



# NASTECH

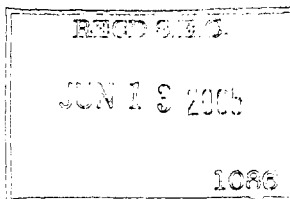
PHARMACEUTICAL COMPANY INC.



05057652

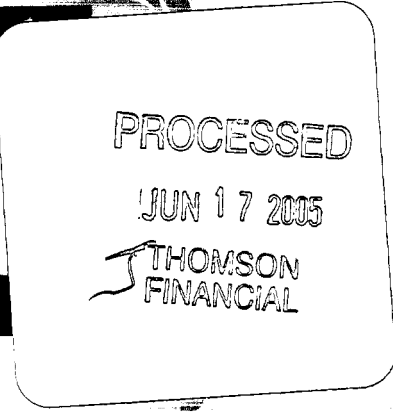
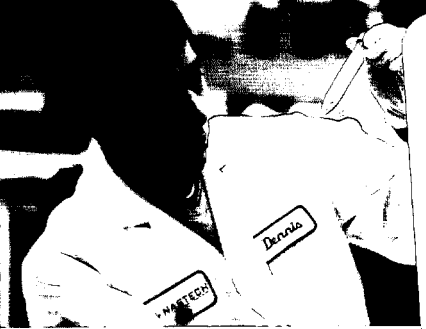
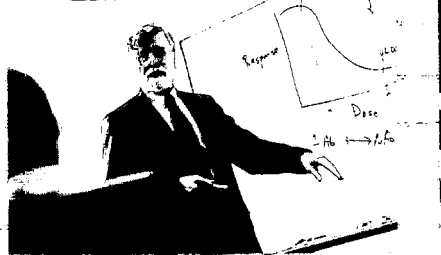
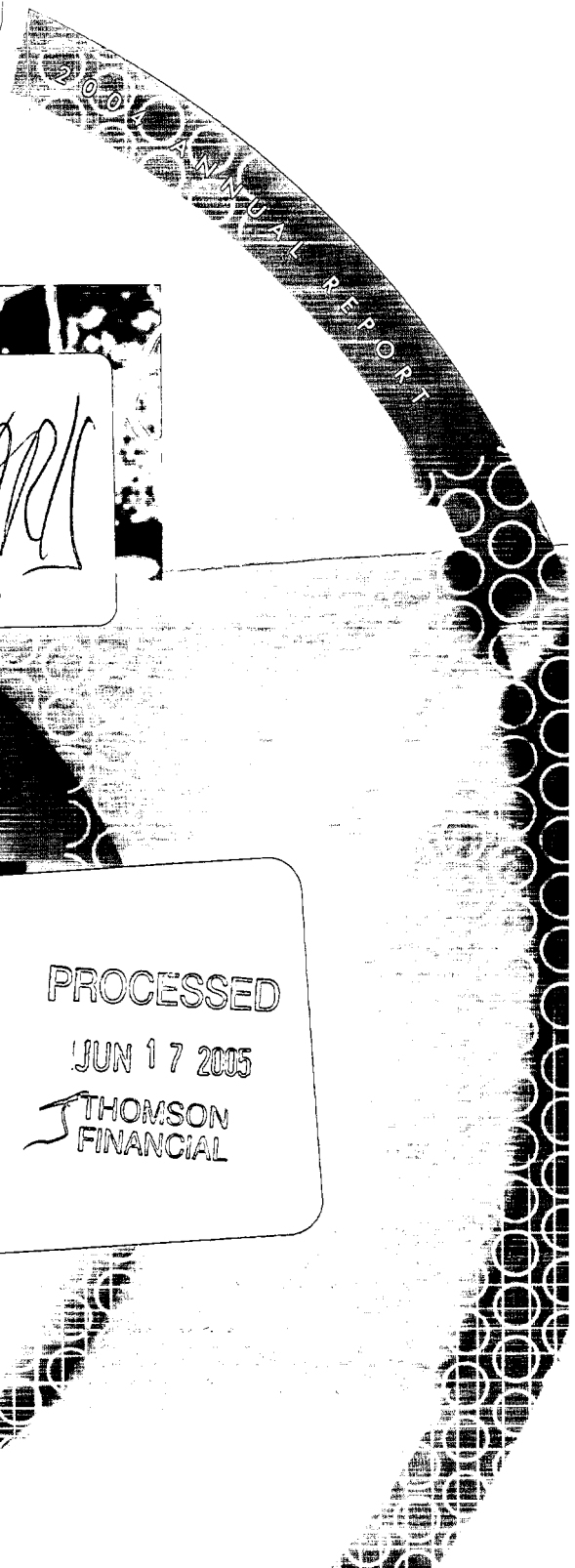
*ARL*

*P.E.  
12/31/04*



*ARL*

0-13789



## MISSION

to develop and commercialize innovative pharmaceutical products based on active delivery molecules in order to effectively transport therapeutic drugs to their disease targets.

## VISION

to improve human health through the development of products that solve complex drug delivery problems and provide superior therapeutic options to patients in need.

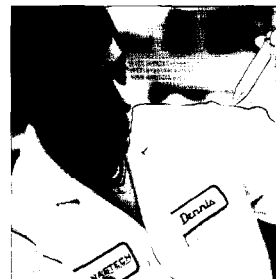
2004 was a pivotal year for Nastech, a year in which the enormous potential of our scientific expertise, technologies and product pipeline was recognized by leading companies in the biopharmaceutical industry. This was highlighted by the signing of a worldwide collaboration with Merck & Co., Inc. (Merck) in September for the development and commercialization of Peptide YY<sub>3-36</sub> (PYY) for obesity. This transaction was an important highlight in a year marked by success across all aspects of our business. I am pleased to share our key accomplishments in 2004 and review our plans to leverage this outstanding success to continue our growth and value creation.

### Building Value Through Partnerships

The collaboration with Merck is our first with a major pharmaceutical company. This partnership is focused on developing and commercializing an exciting new product enabled by our molecular biology based drug delivery technology. It demonstrates that the pharmaceutical industry recognizes our technology and capabilities as a novel solution to their most significant challenge: building a pipeline of proprietary, commercially valuable new drugs, including proteins and peptides.

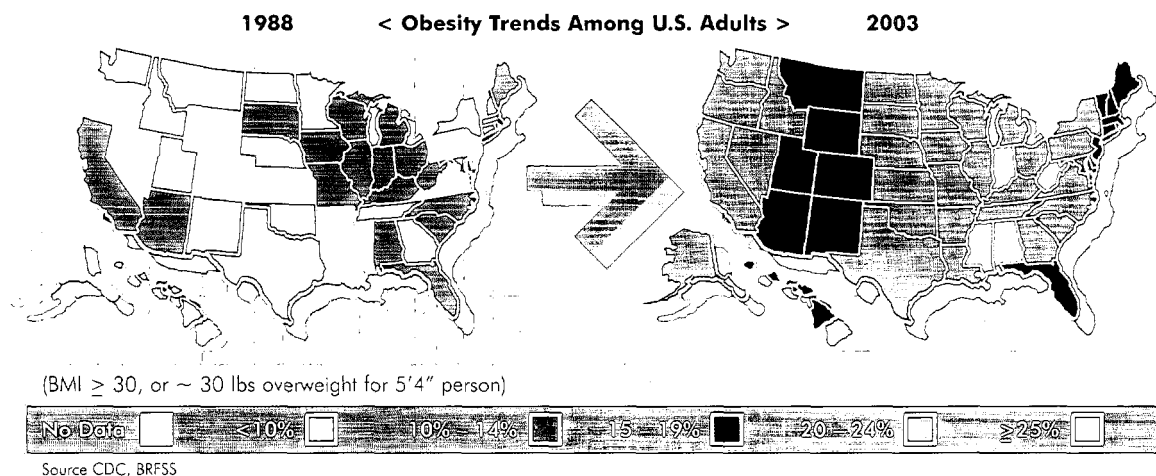
Nastech and Merck are jointly developing PYY. Merck has primary responsibility for clinical and non-clinical studies and regulatory approval, while Nastech is responsible for all manufacturing of PYY-related product. Merck will lead and fund commercialization activities, and we have an opportunity to co-promote PYY in the US. This collaboration also provides us with significant revenue opportunities. We are eligible to receive up to \$131 million in development milestones and up to \$210 million in sales milestones, plus significant royalties on product sales. In addition, Merck will reimburse Nastech for manufacturing-related development activities and will purchase finished product from us upon commercialization. We have established an excellent working relationship with Merck and are pleased with the rapid progress of this program.

Growing recognition of our technology's value has resulted in the signing of several feasibility study agreements with major biopharmaceutical companies in the areas of Type 2 diabetes, Alzheimer's disease and obesity. Our intranasal drug delivery technology enables the development of novel therapies with the potential to improve the lives of millions of patients. We expect to establish additional feasibility programs in 2005, and view these programs as steppingstones to high value, product-focused development and commercialization partnerships.



<sup>66</sup> Growing recognition of our technology's value has resulted in the signing of several feasibility study agreements with major biopharmaceutical companies.<sup>99</sup>

<sup>66</sup> Obesity is a growing epidemic that threatens to reverse rising life expectancy trends. Today, more than 127 million adult Americans (65% of the adult population) are overweight or obese.<sup>99</sup>



“Our partnerships  
are already creating  
value in 2005.”

In October 2004, we leveraged our later-stage product pipeline to create additional value through collaboration. Our commercialization agreement for calcitonin-salmon nasal spray with Par Pharmaceutical combines our capabilities in product development, nasal drug formulation and delivery and commercial-scale nasal manufacturing, with Par's expertise in the sales and marketing of generic pharmaceutical products. We anticipate that this product may capture a significant share of the calcitonin market, approximately \$260 million in the US.

Nastech is responsible for obtaining regulatory approval, manufacturing and providing Par with finished product. Par will exclusively market, sell and distribute the product in the US. We received an upfront payment and may receive regulatory and post-approval milestones, payments for final manufactured product, and a profit sharing arrangement following commercial launch. The terms of the Par agreement underscore the potential of our product pipeline to provide us with near-, mid- and long-term revenue opportunities.

Our partnerships are already creating value in 2005. In February, we announced FDA approval of Nascobal® (Cyanocobalamin, USP) Nasal Spray for the treatment of vitamin B12 deficiency in patients with pernicious anemia, Crohn's Disease, HIV/AIDS, and multiple sclerosis. This approval triggered a \$2 million milestone payment from Questcor Pharmaceuticals, Inc. The approval to market Nascobal within 13 months of submitting our new drug application (NDA) was well under the industry average of 20 months, and demonstrates our ability to successfully manage the regulatory process.

#### Advancing Our Product Pipeline

Our 2004 business development accomplishments were matched by important achievements in our internal product development programs. In April, we initiated clinical development of a nasal spray formulation of parathyroid hormone (PTH), a product already approved and being sold as an injected dosage form for the treatment of osteoporosis. Nastech's program utilizes our tight junction

modulating delivery technology to create a patient-friendly, painless nasal spray dosage form that is designed to increase absorption into the bloodstream and to stimulate bone growth in patients with osteoporosis. Annual sales of the injected form of PTH were in excess of \$200 million in 2004 (NDC Health), and we believe that our non-invasive, intranasal formulation could potentially replace much of the current injected product.



#### PRODUCT PIPELINE:

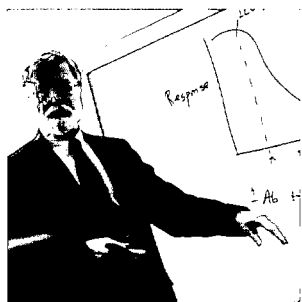
	STAGE					PARTNER
	Pre-Clinical	Phase I	Phase II	Phase III	NDA/ANDA	
Peptide YY <sub>3-36</sub>						MERCK
Obesity						
Parathyroid Hormone (PTH) <sub>1-34</sub>						
Osteoporosis						PAR PHARMACEUTICAL
Calcitonin						
Osteoporosis						
Morphine Glucuronate						BIG PHARMA & BIOTECH
Breakthrough Cancer Pain						
RNAi						
Inflammatory Diseases, Infections, Metabolic Diseases and Cancer Feasibility Studies						
Type II Diabetes, Obesity, and Alzheimer's disease						

PTH is the only FDA-approved anabolic drug for the treatment of osteoporosis and has shown unsurpassed increase in bone mineral density and reduction of fractures in postmenopausal women. In 2004, we completed two Phase I trials of intranasal PTH, generating data that will be used to optimize the formulation we will take into further clinical trials in 2005.

### Innovating Solutions To the Challenges of Drug Development

Our expertise in formulation science and molecular biology-based drug delivery were essential components of our success in 2004 and will be key drivers of future growth. We continue to invest in our core technology as a means to enhance our pipeline and partnership opportunities.

In February 2004, we licensed a portfolio of intellectual property covering RNA interference (RNAi) technology, a powerful new approach to inhibiting the activity of any gene of choice as a way to treat disease. We are using our core strengths in formulation science and molecular biology to develop RNAi therapeutics and new technologies that enable us to deliver them into cells. Our



investment in RNAi technology provides us with near-, mid- and long-term opportunities to improve our existing delivery technologies and expand into new indications, including rheumatoid arthritis, infectious diseases, and cancer.

### Leveraging Our Technology Platforms

Our expertise in molecular biology, formulation science and manufacturing provides a scientific foundation on which to build our diverse product opportunities. These include novel delivery systems for promising therapeutics, such as proteins, peptides, and RNAi molecules. This approach provides us with multiple paths to creating value from our investment in a single set of technologies.

Our tight junction technology is the most advanced of these delivery systems, and is designed to optimize the passage of drugs across epithelial tissue barriers and into the bloodstream by temporarily and reversibly opening tight junctions. The tight junction technology allows Natestech to provide injectable-like performance without the use of a needle. This enabling technology may result in new drugs that have a more rapid onset of action, fewer side effects and the ability to reach previously unavailable drug targets. These properties support the development of new classes of drugs against unique targets and also enable improved formulations of existing drugs. Consequently, our pipeline is diversified both in terms of the product opportunities before us as well as its risk profile.

Nascobal and calcitonin-salmon nasal spray demonstrate that we can create value through the development and commercialization of novel formulations of existing drugs. Our PYY collaboration with Merck and our internal programs exemplify our opportunities to create entirely new therapies that have significant clinical and commercial potential. As we leverage our tight junction technology into near-term revenue from products and partners, we also are advancing development of additional delivery technologies suitable for oral dosage formulations and RNAi molecules. We believe these additional drug delivery systems will provide Natestech with important growth potential.



“We are using our core strengths in formulation science and molecular biology to develop RNAi therapeutics and new technologies that enable us to deliver them into cells.”

66 As a result of our expansion efforts, our intellectual property portfolio comprises more than 200 patents and patent applications.<sup>99</sup>

### Enhancing Our Resources

Throughout 2004 we enhanced our financial and intellectual property resources. In December, we raised \$53 million net through a public offering of common stock. This offering, combined with disciplined management of our existing financial resources and funding from partners, enabled us to end 2004 with \$74.5 million in cash and investments, our strongest cash position ever.

As a result of our expansion efforts, our intellectual property portfolio comprises more than 200 patents and patent applications. We will continue to file patents on our internal discoveries, and pursue additional patented technologies through licenses or acquisitions.

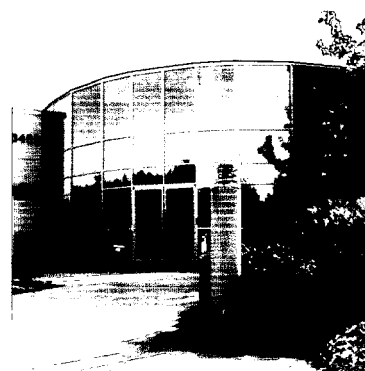
### Focusing On the Future

Our accomplishments in 2004 were a launch pad to our future success, and our 2005 objectives are designed to accelerate value creation for our company, our partners and our shareholders. We will continue to be the best possible partner to Merck, Par and our feasibility study sponsor companies.

We intend to select a PTH formulation for commercialization, and to file an investigational new drug application (IND) with the FDA. We also intend to initiate clinical trials of a previously undisclosed compound during the coming year.

Feasibility studies will provide future product and partnership opportunities, and are a key aspect of our growth strategy. We intend to enter into additional feasibility study agreements in 2005. We also expect to establish a major product collaboration in 2005, either by advancing one of our feasibility programs to a full development agreement, or by partnering one of our legacy programs. Partnerships will continue to be an important component of our strategy to access additional commercialization capabilities and financial resources that will enhance our efforts to bring exciting new products to market.

Our core competency in cutting-edge science will provide the basis for our focus on achieving success with all of our commercial products and programs. These are ambitious objectives, to be sure, but Nastech's success in 2004 demonstrates that we have the strategy, team, partners and resources to achieve our goals. I would like to recognize the contributions that each member of the Nastech team made to our success in 2004. Additionally, I extend our thanks to you, our shareholders for your support of our efforts, and I look forward to sharing our progress with you in the months ahead.



**Steven C. Quay, M.D., Ph.D.**

Chairman, President & Chief Executive Officer

June 2005

Dear Shareholders:

As I look back on the past year, I am proud of the progress we have made in 2004. We have achieved significant milestones in our research and development efforts, and we are excited about the future of our company.

Our focus on enhancing our resources and focusing on the future has allowed us to achieve our goals. We have a strong financial position and a robust intellectual property portfolio. We are confident that we will continue to achieve success in the years ahead.

I would like to thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

Thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

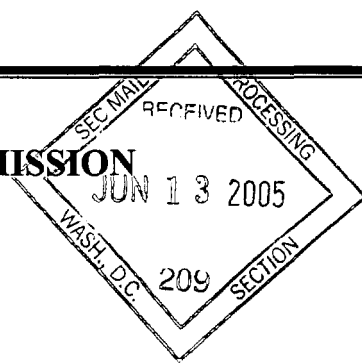
Thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

Thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

Thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

Thank you for your support and confidence in us. We will continue to work hard to create value for our shareholders and partners.

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549



**FORM 10-K/A  
(Amendment No. 1)**

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES  
EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2004  
Commission File Number 0-13789

**NASTECH PHARMACEUTICAL COMPANY INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**11-2658569**  
(I.R.S. Employer Identification No.)

**3450 Monte Villa Parkway  
Bothell, Washington**  
(Address of principal executive offices)

**98021**  
(Zip Code)

**Registrant's telephone number, including area code: (425) 908-3600**

**Securities registered pursuant to Section 12(b) of the Act:**

Title of each class  
None

Name of each exchange  
on which registered  
None

**Securities registered pursuant to Section 12(g) of the Act:**

Title of each class  
Common Stock, \$0.006 par value  
Preferred Stock Purchase Rights, \$0.01 par value

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the Registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes ☒ No ☐

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of June 30, 2004 based upon the closing price on that date, on the Nasdaq National Market, was approximately \$122,400,000.

As of February 28, 2005, there were 17,930,854 shares of the Registrant's \$0.006 par value common stock outstanding.

# **NASTECH PHARMACEUTICAL COMPANY INC.**

## **Table of Contents**

	<u>Page</u>
 <b>PART I</b>	
Item 1. Business	4
Item 2. Properties	31
Item 3. Legal Proceedings	32
Item 4. Submission of Matters to a Vote of Security Holders	32
 <b>PART II</b>	
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	33
Item 6. Selected Financial Data	34
Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations	35
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	48
Item 8. Financial Statements and Supplementary Data	49
Item 9. Changes In and Disagreements With Accountants on Accounting and Financial Disclosure	74
Item 9A. Controls and Procedures	74
Item 9B. Other Information	75
 <b>PART III</b>	
Item 10. Directors and Executive Officers of the Registrant	75
Item 11. Executive Compensation	79
Item 12. Security Ownership of Certain Beneficial Owners and Management	88
Item 13. Certain Relationships and Related Transactions	90
Item 14. Principal Accounting Fees and Services	91
 <b>PART IV</b>	
Item 15. Exhibits, Financial Statement Schedules	92
Signatures	93
Exhibit Index	94



## EXPLANATORY NOTE

We are filing this Amendment No. 1 to our Form 10-K for the fiscal year ended December 31, 2004, originally filed with the Securities and Exchange Commission on March 8, 2005 (the "Original Form 10-K"), for the purpose of including information required by Part III, Items 10, 11, 12, 13, and 14, which was previously incorporated by reference to our Definitive Proxy Statement for our 2005 annual meeting of stockholders, as well as to make certain other technical corrections. No attempt has been made in this Amendment No. 1 to materially modify or update other disclosures presented in the Original Form 10-K, except as required to reflect the information as indicated above. While we are amending only certain portions of the Original Form 10-K, for convenience and ease of reference, we are filing the entire Form 10-K with this Amendment No. 1 in an amended and restated format, excluding all exhibits other than Exhibits 23.1, 31.1, 31.2, 32.1, and 32.2. This Amendment No. 1 does not reflect events occurring after the filing of the Original Form 10-K or modify or update those disclosures, including the exhibits to the Original Form 10-K, affected by subsequent events. Information not affected by the information is unchanged and reflects the disclosures made at the time of the filing of the Original Form 10-K on March 8, 2005.

## FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K/A and the documents incorporated herein by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These forward-looking statements reflect our current views with respect to future events or our financial performance, and involve certain known and unknown risks, uncertainties and other factors, including those identified below, which may cause our or our industry's actual or future results, levels of activity, performance or achievements to differ materially from those expressed or implied by any forward-looking statements or from historical results. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements include information concerning our possible or assumed future results of operations and statements preceded by, followed by, or that includes the words "may," "will," "could," "would," "should," "believe," "expect," "plan," "anticipate," "intend," "estimate," "predict," "potential" or similar expressions.

Forward-looking statements are inherently subject to risks and uncertainties, many of which we cannot predict with accuracy and some of which we might not even anticipate. Although we believe that the expectations reflected in such forward-looking statements are based upon reasonable assumptions at the time made, we can give no assurance that such expectations will be achieved. Future events and actual results, financial and otherwise, may differ materially from the results discussed in the forward-looking statements. Readers are cautioned not to place undue reliance on these forward-looking statements. We have no duty to update or revise any forward-looking statements after the date of this report or to conform them to actual results, new information, future events or otherwise.

The following factors, among others, could cause our or our industry's future results to differ materially from historical results or those anticipated:

- our ability to obtain additional funding;
- our efforts to establish and maintain collaboration partnerships for the development of PYY intranasal spray, PTH<sub>1-34</sub>, generic calcitonin-salmon intranasal spray, apomorphine HCl intranasal spray, morphine gluconate intranasal spray, beta interferon, abuse-resistant opioid or other programs;
- the success or failure of our research and development programs;
- the advantages and disadvantages of pharmaceuticals delivered intranasally;
- the need for improved and alternative drug delivery methods;

- our efforts to collaborate with other pharmaceutical and biotechnology companies that have products under development;
- our ability to successfully complete product research and development, including pre-clinical and clinical studies, the U.S. Food and Drug Administration (“FDA”) and foreign equivalent approvals, current Good Manufacturing Practices (“cGMP”), and commercialization;
- our ability to obtain governmental authorizations, including product approvals and patent issuances;
- our ability to successfully manufacture the products of our research and development programs and our marketed products to meet cGMP and to manufacture these products at a financially acceptable cost;
- our ability to attract and retain our key officers and employees and manufacturing, sales, distribution and marketing partners;
- costs associated with any product liability claims, patent prosecution, patent infringement lawsuits and other lawsuits;
- our ability to develop and commercialize our products before our competitors; and
- the projected size of the drug delivery market in general and the market for our projects and programs specifically.

We assume no obligation to update and supplement forward-looking statements that become untrue because of subsequent events.

These factors and the risk factors included in this Annual Report on Form 10-K/A under Item 1 - Business — Risk Factors, are all of the important factors of which we are currently aware that could cause actual results, performance or achievements to differ materially from those expressed in any of our forward-looking statements. We operate in a continually changing business environment, and new risk factors emerge from time to time. Other unknown or unpredictable factors also could have material adverse effects on our future results, performance or achievements. We cannot assure you that projected results or events will be achieved or will occur.

## **PART I**

### **ITEM 1. BUSINESS**

#### **Overview**

We are a pharmaceutical company focusing on development and commercialization of innovative products based on proprietary molecular biology-based intranasal drug delivery technology for delivering both small and large molecule drugs. Using this technology, we create or utilize novel formulation components or excipients that can transiently manipulate or open “tight junctions” between cells in various tissues and thereby allow therapeutic drugs to reach the blood stream. Tight junctions are cell-to-cell connections in various tissues of the body, including epithelial and endothelial layers of the intranasal mucosa, the gastrointestinal tract, and the blood brain barrier. They function to provide barrier integrity and to regulate the transport and passage of molecules across these natural boundaries. This technology is the foundation of our intranasal drug delivery platform, although some of our product candidates utilize our expertise outside this area. Generally, we seek to apply our technology to compounds that we license to, or acquire from, collaborators or other third parties.

We believe our intranasal drug delivery technology offers advantages over injectable routes for the administration of large molecules such as peptides and proteins. These advantages may include improved safety and

clinical efficacy and increased patient compliance due to the elimination of injection site pain and avoidance of injection site irritation. In addition, we believe our intranasal drug delivery technology offers advantages over oral administration by providing for faster absorption into the bloodstream, reduced side effects and improved effectiveness by avoiding problems relating to gastrointestinal and liver metabolism. We are utilizing our technologies to develop commercial products, initially with collaboration partners. In select cases, we also plan to internally develop, manufacture and commercialize our products.

We and our collaboration partners are developing a diverse portfolio of product candidates for multiple therapeutic areas including obesity, osteoporosis, breakthrough cancer pain, multiple sclerosis and erectile dysfunction. Our lead product candidate, Peptide YY<sub>3-36</sub> ("PYY") for obesity, is in Phase I clinical trials and is being developed with our collaboration partner Merck & Co. Inc. ("Merck"). Additionally, we are developing two product candidates for the treatment of osteoporosis. Parathyroid Hormone PTH<sub>1-34</sub> ("PTH<sub>(1-34)</sub>") is in Phase I clinical trials, and we have filed an abbreviated new drug application ("ANDA") for our generic calcitonin-salmon intranasal spray which we are developing with our collaboration partner Par Pharmaceutical Inc. ("Par Pharmaceutical"). As of February 15, 2005, we have 41 patents issued and 161 patent applications filed to protect our proprietary technologies.

### Product Candidates

The following table summarizes the current status of our clinical-stage product candidates.

<u>Product</u>	<u>Initial Indication</u>	<u>Clinical Status</u>	<u>Next Steps</u>	<u>Marketing Rights</u>	<u>Delivery Technology/Intellectual Property</u>
Peptide YY <sub>(3-36)</sub>	Obesity	Three Phase I studies completed. An additional Phase I study began in January 2005.	Joint development with Merck conducting clinical and pre-clinical studies and Nastech performing manufacturing activities	Merck (world-wide) Nastech (co-promotion rights in the U.S.)	Tight junction/ patents and applications PYY patents and applications
Parathyroid Hormone PTH <sub>(1-34)</sub> (Peptide)	Osteoporosis	Two Phase I studies completed	Pre-clinical and Phase I clinical studies	Nastech	Tight junction/patents and applications
Calcitonin-salmon (Peptide)	Osteoporosis	ANDA submitted and accepted for review by the FDA	FDA review of ANDA	Par Pharmaceutical (U.S.) Nastech (rest of world)	Other/formulation patent applications
Apomorphine HCl (Small molecule)	Erectile dysfunction	Four Phase II studies completed	Currently seeking a partner	Nastech	Other/formulation patents and applications
Morphine Gluconate (Small molecule)	Breakthrough cancer pain	One Phase II study completed	Currently seeking a partner	Nastech	Other/formulation patents and applications
Beta Interferon (Protein)	Multiple sclerosis	One Phase I study completed	Currently seeking a partner	Nastech	Tight junction/ patents and applications

## **Obesity**

Obesity is a chronic condition that affects millions of people worldwide and often requires long-term or invasive treatment to promote and sustain weight loss. According to recent estimates from the National Institutes of Health, nearly two-thirds of U.S. adults are overweight and nearly one-third are obese. Obesity among adults has doubled in the past two decades. Research studies have shown that obesity increases the risk of developing a number of adverse conditions including Type 2 Diabetes, hypertension, coronary heart disease, ischemic stroke, colon cancer, post-menopausal breast cancer, endometrial cancer, gall bladder disease, osteoarthritis and obstructive sleep apnea.

### *Peptide YY<sub>(3-36)</sub>*

PYY, a high affinity Y2 receptor agonist, may represent a new approach to the treatment of obesity. This hormone is naturally produced in the abdomen by specialized endocrine cells in proportion to the caloric content of a meal and is believed to reduce food intake by modulating appetite responses in the hypothalamus. Results from a study conducted by Dr. Stephen R. Bloom and colleagues published in *The New England Journal of Medicine* (September 4, 2003, Volume 349, Number 10, Pages 941-948), found that obese subjects had lower levels of PYY than non-obese subjects, suggesting that PYY deficiency may contribute to the pathogenesis of obesity and that PYY supplementation may have therapeutic benefit. The study further demonstrated a 16.5% calorie reduction in obese subjects for the 24-hour period following a single intravenous injection of PYY, based on diary recorded food intake. We have developed a proprietary intranasal formulation of PYY and have filed patent applications containing over 350 claims in the U.S. and seven other countries, and an International Patent Application in which all countries were designated. We and Merck are currently in Phase I clinical trials with this program.

On September 24, 2004, we entered into an exclusive development, commercialization and license agreement and a separate exclusive supply agreement with Merck for the development and commercialization of PYY intranasal spray for the treatment of obesity. The collaborative arrangement provides that Merck will assume primary responsibility for conducting and funding pre-clinical and clinical studies and regulatory approvals, while we will be responsible for all manufacturing of PYY-related product. Merck will lead and fund world-wide commercialization, and we have the right to co-promote the product in the United States.

Under the collaborative arrangement with Merck, we received an initial cash payment of \$5 million in October 2004. The \$5 million initial payment is being amortized over the estimated development period of the product candidate. We are also eligible to receive milestone payments upon our achievement of specified product development goals or sales targets. If certain development and approval milestones are achieved, we will be eligible to receive up to \$131 million from Merck. If certain sales related milestones are achieved, we will be eligible to receive up to an additional \$210 million from Merck subject to certain other conditions. Merck will also pay us for manufacturing-related development activities and will purchase from us all clinical supply and finished product. We will also receive royalties on product sales based on certain sales-related thresholds.

We believe our collaboration with Merck demonstrates we have taken a significant step toward becoming a leader in the development of innovative, intranasal drug delivery products and technologies. We also believe this collaboration partnership demonstrates the value PYY holds as a potential treatment option for obesity.

We believe we possess a broad and effective PYY intellectual property estate, which includes the combination of:

- our own patent estate containing ten pending U.S. patent applications and nine pending foreign patent applications;
- an exclusive license to the Cedars-Sinai patent estate secured earlier this year containing the only issued patent directed to the use of PYY or functional analogs to induce satiety;

- our acquisition of exclusive worldwide rights to the PYY patent applications within the field of intranasal administration, licensed from Imperial College and Oregon Health Sciences University through Thiakis Limited ("Thiakis"); and
- our acquisition of an exclusive license to five issued patents and two pending applications from the University of Cincinnati related to second generation PYY analogs that have produced weight loss in animal experiments.

We have sublicensed the rights to the development and commercialization of this portfolio, except for the recent license obtained from the University of Cincinnati, exclusively to Merck as part of our alliance with Merck.

**Clinical Trial Data.** We have completed three Phase I studies, each designed to answer specific dosing, scheduling and tolerance questions. To date, we have enrolled over sixty subjects and administered over 900 doses in the PYY program.

In a Phase IA dose ranging study of 15 healthy subjects, intranasal administration of PYY resulted in blood levels which equaled or exceeded normal post-meal PYY levels. The half-life of PYY was approximately one hour, which is similar to what occurs naturally after a meal. The safety profile was encouraging with no intranasal discomfort and no significant vital sign changes in any subject.

In a Phase IB dose finding study of 12 otherwise healthy overweight subjects, intranasal administration of PYY statistically significantly reduced, in the nine responding subjects, appetite and caloric intake both at the lunch meal 60 minutes after administration, as well as for the entire 24-hour period following administration. Two subjects did not respond and a third subject withdrew because of unrelated complications. Side effects were generally mild and all resolved without treatment. Based on this data, we believe the intranasal formulation of PYY effectively increases plasma concentrations of this peptide following a single dose, and is safe and well tolerated at all dose levels tested.

In a Phase IC dose sequencing study of 36 otherwise healthy obese subjects, the subjects received placebo or PYY once, twice or three times daily one hour before each meal for eight consecutive days. The study showed that 24-hour caloric reduction over all days of treatment was related to the number of daily PYY administrations, with those receiving one dose experiencing a mean reduction of 77 calories per day, two doses experiencing a mean reduction of 197 calories per day, and those receiving PYY three times daily experiencing a mean reduction of 490 calories per day. Subjects receiving PYY three times a day recorded a weight reduction of 1.3 pounds over the last six days of the study. PYY was well tolerated, with the only side effects at one percent or greater being nausea, headache and dizziness. Nausea was reported by subjects in 11% of the PYY doses administered, headache in 5% and dizziness in 1%. We believe the intranasal formulation of PYY effectively increases plasma concentrations of this peptide following a dose of 200 micrograms, and was found to be safe and well tolerated at dose levels up to 600 micrograms per day.

**Current Initiatives.** We and Merck are working together to advance PYY into additional pre-clinical and clinical studies. A product development team with employees from both companies is working on all aspects of the PYY product development program, with Merck overseeing all critical decisions. Merck will be primarily responsible for conducting such studies and obtaining regulatory approval throughout the world. On January 26, 2005, we announced that Merck initiated a Phase I study for PYY intranasal spray for the treatment of obesity. This study, being conducted by Merck, builds upon our previous PYY clinical programs, under which 63 subjects have received more than 900 doses of intranasal PYY prior to Merck's initiation of this study.

### ***Osteoporosis***

Osteoporosis is the development of low bone mass that compromises bone strength and increases the risk of bone fracture. According to Datamonitor, the osteoporosis pharmaceutical market is currently \$7 billion and is expected to grow as the population ages. PTH<sub>(1-34)</sub> is the only product that has been shown in clinical trials to build

bone rather than only slowing its rate of loss. Currently, Eli Lilly and Company's ("Eli Lilly") Forteo is the only commercially available PTH<sub>(1-34)</sub> therapy approved for the treatment of post-menopausal osteoporosis in women as well as osteoporosis in men. Despite the cost and the requirement for daily injections into the thigh or abdomen, according to NDC Pharmaceutical Audit Suite (PHAST) January-December 2004 data including pharmaceutical prescription purchases at wholesale acquisition cost (WAC) price for retail, mail order, clinics, hospitals, long-term care and home healthcare organizations and other non-retail channels (the "NDC Report"), Forteo recorded U.S. sales revenue of approximately \$205 million in 2004.

In addition, Novartis AG's ("Novartis") Miacalcin, a currently approved and marketed intranasal calcitonin-salmon spray, has been shown to increase spinal bone mass in post-menopausal women with established osteoporosis and is the only osteoporosis treatment specifically labeled to be used for women for whom estrogens are contraindicated. According to the NDC Report, Miacalcin had U.S. sales of approximately \$260 million in 2004.

#### *Parathyroid Hormone PTH<sub>(1-34)</sub>*

PTH<sub>(1-34)</sub> is part of the naturally occurring human parathyroid hormone that helps regulate calcium and phosphorus metabolism. We have developed a proprietary intranasal formulation of PTH<sub>(1-34)</sub> and have filed two U.S. patent applications containing an aggregate of 103 claims. We are currently in Phase I clinical trials in this program. We view a potentially non-invasive, intranasally delivered alternative to Forteo as a significant market opportunity.

**Clinical Trial Data.** Our clinical program was launched in the second quarter of 2004 and two Phase I clinical trials have been completed with PTH<sub>(1-34)</sub>. Our clinical studies to date provide the basis for formulation optimization of our PTH<sub>(1-34)</sub> intranasal spray, which is the next step in the program.

**Current Initiatives.** The next step in the clinical development of our PTH<sub>(1-34)</sub> program will be formulation optimization of our intranasal PTH<sub>(1-34)</sub> and clarification with the FDA on the regulatory path and studies needed for product approval, which will result in a candidate formulation to be taken forward in pre-clinical and clinical trials.

#### *Calcitonin-Salmon*

Calcitonin is a natural peptide hormone produced by the thyroid gland that acts primarily on bone. Bone is in a constant state of remodeling, whereby old bone is removed and new bone is created. Calcitonin inhibits bone removal and thereby promotes bone formation. Calcitonin-salmon appears to have actions essentially identical to calcitonins of mammalian origin, but its potency is greater due to a longer duration of action. We believe that our calcitonin-salmon intranasal spray could be a generic alternative to Novartis' Miacalcin.

**Clinical Trial Data.** In December 2003, we filed with the U.S. Food and Drug Administration ("FDA") an ANDA for generic calcitonin-salmon intranasal spray for osteoporosis. As part of the ANDA process, we have conducted a clinical trial and laboratory tests including spray characterization and spray content, designed to demonstrate the equivalence of our product to the currently marketed drug, Miacalcin. In February 2004, the FDA accepted the filing of our ANDA for the product. In June 2004, we announced that the FDA had conducted a successful Pre-Approval Inspection of our generic calcitonin-salmon intranasal spray manufacturing facility with no cited deviations from cGMP. At this time, we believe that we have provided the FDA with a complete written response to all of its questions relating to this ANDA.

**Current Initiatives.** The calcitonin-salmon intranasal spray ANDA has been submitted and accepted for review by the FDA.

#### *Erectile Dysfunction*

Erectile dysfunction has been estimated to affect up to 30 million men in the United States alone according to a study published in *The New England Journal of Medicine* (June 15, 2000, Volume 342, Number 24, Pages 1802-

1813). In the Massachusetts Male Aging Study, based on a cross sectional, community-based, random sample survey of 1,300 men aged between 40 and 70 years, 52% of men were found to have some degree of erectile dysfunction. According to the NDC Report, in 2004 the three leading drugs in the U.S. erectile dysfunction market accounted for approximately \$1.2 billion in sales.

#### *Apomorphine Hydrochloride*

Apomorphine Hydrochloride ("HCl") is a centrally acting dopamine agonist that enhances nerve signals sent by the brain during sexual stimulation. Dopamine agonists mimic the body's natural neurotransmitter, dopamine, to affect an erection via the brain and spinal cord where other currently marketed pharmaceuticals for the treatment of erectile dysfunction treat the disorder peripherally by dilating the vasculature and increasing blood flow to produce an erection. The subcutaneous injection of apomorphine has been shown to induce erections in men with erectile dysfunction. Marketing authorization for sublingual apomorphine HCl for erectile dysfunction was granted in Europe in May 2001. We believe that we have developed an intranasal formulation of apomorphine HCl which allows for easier use than subcutaneous administration and may allow lower doses and reduced side effects compared to the commercialized sublingual formulation.

In February 2002, we granted Pharmacia & Upjohn Company ("Pharmacia") exclusive, worldwide rights to develop and market intranasal apomorphine for the treatment of male and female sexual dysfunction, and Pharmacia agreed to manage and fund all future development in these indications. In January 2003, the Federal Trade Commission mandated as part of the Pfizer/Pharmacia merger that Pharmacia divest its apomorphine HCl product. As a result of the Federal Trade Commission mandate, we entered into a divestiture agreement with Pharmacia under which we reacquired assets related to the intranasal apomorphine product that we had originally granted to Pharmacia in February 2002.

**Clinical Trial Data.** In November 2001, we completed a Phase II clinical trial in 184 men with erectile dysfunction. In March 2004, we announced the successful completion of a maximum tolerated dose study for this program. The multi-center, double blind, placebo-controlled study enrolled 102 men age 50 to 82 years, approximately half of whom had erectile dysfunction. The study involved a single daily active- or placebo-dose administration for seven consecutive days. Doses began at 0.5 mg and escalated in increments of 0.25 mg. Vital signs were measured both supine and standing to observe orthostatic effects and echocardiogram measurements were taken during the five hours after each dose.

Based on the results of this study, we believe that doses up to 1.75 mg are safe and well tolerated and doses up to 2.0 mg are acceptable for further in-clinic safety studies. All safety findings will need to be confirmed as part of the ongoing clinical development of apomorphine HCl.

**Current Initiatives.** We are seeking a collaboration partner for further development of the apomorphine HCl program.

#### ***Breakthrough Cancer Pain***

In addition to their usual pain, cancer patients frequently experience breakthrough pain, a transitory exacerbation that occurs over a background of otherwise stable pain. Breakthrough cancer pain can occur several times daily, is rapid in onset and unpredictable in time of occurrence and frequency. Oral opioids do not have optimal clinical characteristics for use in the treatment of breakthrough cancer pain due to their slow onset of action of approximately 45 to 120 minutes. Breakthrough cancer pain is one of the most commonly experienced symptoms of advanced cancer, affecting over three million people in the U.S. annually. According to Datamonitor, the worldwide market for breakthrough pain in cancer patients represents approximately \$1 billion. Currently, only Cephalon, Inc.'s ("Cephalon") Actiq, a transmucosal oral fentanyl product, is approved for treating breakthrough cancer pain for opioid-tolerant cancer patients. According to the NDC Report, Actiq recorded sales revenue of approximately \$335 million in 2004.

## *Morphine Gluconate*

Morphine is a well known opioid analgesic currently marketed in multiple dosage forms including those for injectable, oral and rectal administration. We believe that an intranasal dosage form of our patented morphine gluconate, an enhanced bioavailable form of morphine, will enable patient-friendly self-administration and provide a rapid systemic absorption of the drug for fast pain relief, particularly among patients with breakthrough cancer pain. We have developed a proprietary formulation of morphine gluconate and completed a Phase II clinical trial.

**Clinical Trial Data.** In December 2003, Dr. Fitzgibbon of the University of Washington, the principal investigator, and his colleagues published the results from a Phase II clinical trial in patients with breakthrough cancer pain, indicating that intranasal morphine gluconate was rapidly absorbed, with onset of pain relief at an average of 2.2 minutes post dosing and meaningful pain relief at an average of 9.1 minutes (*Pain*, December 2003, volume 106, pages 309-315). There was a statistically significant difference between baseline pain intensity versus post dose pain intensity (p 0.05). None of the patients needed to take another breakthrough pain medication within 30 minutes after dosing, and 64% of the patients did not need rescue medication within the first hour. There were no serious adverse events reported.

**Current Initiatives.** We are seeking a collaboration partner for further development of this product.

## *Multiple Sclerosis*

Multiple sclerosis is a chronic autoimmune disease characterized by demyelination of nerve fibers, leading to nerve damage and associated symptoms of fatigue, cognitive and visual impairments. Currently, five drugs have been approved for the treatment of multiple sclerosis. Beta interferon is the most commonly prescribed treatment for multiple sclerosis with U.S. sales of approximately \$1.1 billion in 2004 according to the NDC report.

## *Beta Interferon*

Interferons are a family of naturally occurring proteins and glycoproteins classified as cytokines. They are produced by cells in response to viral infection and other biological inducers and mediate antiviral, antiproliferative and immunomodulatory activities. Beta interferon is currently administered by injectable dosage form only. We believe that an intranasal dosage form would potentially increase patient compliance and efficacy with fewer side effects compared to an injectable product. We have developed a proprietary intranasal formulation of beta interferon and have completed a Phase I clinical trial to date.

**Clinical Trial Data.** At the annual meeting of the American Academy of Neurology in April 2004, we reported positive results from the Phase I clinical trial in healthy male subjects. When compared to injection, the intranasal formulation shows relative potency of approximately 20%. All three subjects who received the injection administration reported fever, one reported chills and one reported headache. Following intranasal administration, four of 11 subjects reported intranasal symptoms, three of 11 reported unusual taste, one of 11 reported headache and one of 11 reported shortness of breath. There were no neutralizing antibodies to beta interferon identified at six months after dosing. With additional formulation optimization, we believe that the intranasal formulation should be appropriate for dosing every other day or three times a week.

**Current Initiatives.** We are seeking a collaboration partner for further development of this product.

## **Pre-Clinical Program**

### *Abuse-Resistant Opioid*

Our abuse-resistant opioid is a chemically-modified prodrug of oxycodone. We believe that this prodrug formulation has decreased abuse potential. When taken orally, our abuse-resistant opioid is metabolized by enzymes and other agents in the small intestine and results in the slow release of opioid over time. Our abuse-resistant opioid



is currently in pre-clinical development, including pharmacokinetic studies to support further pre-clinical and possible clinical development. We are seeking to partner this potential advancement in oral narcotic pain management. According to the NDC Report, in 2004, Purdue Pharma L.P. ("Purdue") recorded U.S. sales for Oxycontin in excess of \$1.7 billion.

## **Feasibility Studies**

We are participating in three funded, feasibility studies with three different research partners to evaluate the development of proprietary formulations for the intranasal delivery of an injected compound for the treatment of Type 2 Diabetes, an oral compound for the treatment of Alzheimer's disease and a compound not related to PYY for the treatment of obesity. We will utilize our proprietary tight junction technology to develop intranasal formulations of each of these compounds. In vitro laboratory testing of toxicity and permeability of formulations and pre-clinical studies to assess the pharmacokinetics and safety of the intranasally delivered formulations compared to current injectable or oral dosage forms will be performed.

## **Drug Delivery Technologies**

### ***Tight Junction Technology***

We focus on molecular-biology based drug delivery, which involves the use of gene cloning, high throughput tissue culture screening, phage display selection, RNA interference (RNAi) gene function knockdown, and peptide synthesis to create novel formulation components or excipients that can transiently manipulate or open "tight junctions" and thereby allow therapeutic drugs to reach the blood stream. Tight junctions are cell-to-cell connections in various tissues of the body, including epithelial and endothelial layers of the intranasal mucosa, the gastrointestinal surface, and the blood brain barrier. They function to provide barrier integrity and to regulate the transport and passage of therapeutic drugs across these natural boundaries. As part of the body's normal activity, tight junctions selectively open and close in response to various signals inside and outside of cells allowing the passage of large molecules or even entire cells across the tight junction barrier.

Tight junctions are found in all tissues, but the tight junction containing tissues that are of particular relevance to drug delivery are found in intranasal tissue, intestinal tissue, blood vessels, and the blood-brain barrier. The blood-brain barrier is a specialized layer of endothelial cells that line the inner surface of blood vessels in the brain, which excludes many drugs from passing into the brain. Drugs, particularly those utilizing large molecules, need to pass through these tissue barriers in order to get to their sites of action.

Tight junctions consist of proteins, such as claudins, occludin and junctional adhesion molecules that are anchored in the membranes of two adjacent cells and interact with each other to hold the cells together and prevent other molecules from passing between them.

The goal of our tight junction biology program is to understand the structure and function of these tissue barriers and to identify active compounds that can transiently open the tight junction, thus permitting drugs to pass through. We have genetically engineered and produced many of the key tight junction proteins and are using them as targets to identify peptides and small molecules that can significantly improve drug delivery by temporarily opening these tight junctions. We call such peptides and small molecules "tight junction modulators."

By improving our understanding of the structure and function of tight junctions in the intranasal epithelial barrier, we expect to continue to make significant improvements in the delivery of both small and large molecules for an increasing number of therapeutic applications. We believe our intranasal drug delivery technology will offer advantages over injectable routes for the administration of large molecules such as peptides and proteins. These advantages may include improved safety and clinical efficacy and increased patient compliance due to elimination of injection site pain and avoidance of injection site irritation. In addition, we believe our intranasal drug delivery technology will offer advantages over oral administration by providing for faster absorption into the bloodstream,

reduced side effects like nausea and vomiting and improved effectiveness by avoiding problems relating to gastrointestinal and liver metabolism.

Through our tight junction technology, we have identified compounds that directly and specifically affect the tight junctions between cells in the intranasal tissues in a manner mimicking natural processes (for example, the effects are reversible) and result in increasing drug permeability through the tight junction barrier. Based on these approaches, we have developed formulations for improving the delivery of promising new classes of drugs such as PYY for the treatment of obesity, PTH<sub>(1-34)</sub> for the treatment of osteoporosis and beta interferon for the treatment of multiple sclerosis. We believe that we were the first to demonstrate delivery of PYY by a non-injected route.

We believe that our tight junction technology has significant potential applications outside of intranasal drug delivery, particularly for improving oral drug delivery (through the gastrointestinal tract), intravenous drug delivery (through blood vessel walls into tissues), and drug delivery through the blood brain barrier (through the blood to the brain) for the treatment of diseases. All of these tissue barriers have tight junctions which, although distinct, have properties in common that can be manipulated by the technology we are developing.

RNAi is an important tool we are using to analyze tight junction function and to determine the importance of individual tight junction proteins in affecting drug delivery. RNAi is double-stranded RNA molecules 20-22 nucleotides in length that are able to silence a specific gene and reduce the amount of the protein the gene produces. We have developed RNAi against a number of the tight junction proteins and determined the resulting effects on the tight junction. For example, we can determine whether RNAi inhibition of specific tight junction proteins increases tight junction permeability. These types of studies help to identify which tight junction components are the most appropriate targets to affect in order to improve the passage of drugs through tissue barriers.

#### ***Other Drug Delivery Technologies***

In addition to the use of RNAi as a research tool, we are focusing considerable attention at Nastech on the use of RNAi as a therapeutic strategy to decrease levels of disease-associated proteins. The application of RNAi in this manner requires the ability to deliver the RNAi inside the cells where the target proteins are produced. We have established a research and development program to enhance systematic delivery of this potential new class of therapeutics.

Other expertise that we utilize in identifying and developing product candidates include:

- manufacturing know-how;
- experience stabilizing liquid formulations;
- knowledge of physical properties of intranasal sprays;
- experience with prodrug selection to improve biological properties;
- experience with counter ion selection to increase drug solubility; and
- correlations between in vitro and in vivo intranasal delivery models.

#### **Strategic Collaborations**

We seek to establish and maintain strategic collaborations to commercialize many of our product candidates, including by providing the regulatory compliance, sales, marketing and distribution capabilities required for the success of our business. The decision to seek a collaboration partner for a product candidate is affected by a number of variables, including our specific expertise with the product candidate, the expected cost of development, our

existing product candidates, and our available human and capital resources. Our current collaborative arrangements are as follows:

#### ***Merck***

On September 24, 2004, we entered into an exclusive development, commercialization and license agreement and a separate exclusive supply agreement with Merck for the development and commercialization of PYY intranasal spray for the treatment of obesity. The collaborative arrangement provides that Merck will assume primary responsibility for conducting and funding pre-clinical and clinical studies and regulatory approvals, while we will be responsible for all manufacturing of PYY-related product. Merck will lead and fund world-wide commercialization, and we have the right to co-promote the product in the United States.

Under the collaborative arrangement with Merck, we received an initial cash payment of \$5 million in October 2004. The \$5 million initial payment is being amortized over the estimated development period. We are also eligible to receive milestone payments upon our achievement of specified product development goals or sales targets. If certain development and approval milestones are achieved, we will be eligible to receive up to \$131 million from Merck. If certain sales related milestones are achieved, we will be eligible to receive up to an additional \$210 million from Merck subject to certain other conditions. Merck will also pay us for manufacturing-related development activities and will purchase from us all clinical supply and finished product. We will also receive royalties on product sales based on certain sales-related thresholds.

We believe our collaboration with Merck demonstrates we have taken a significant step toward becoming a leader in the development of innovative, intranasal drug delivery products and technologies. We also believe that this collaboration partnership demonstrates the value PYY holds as a potential treatment option for obesity.

#### ***Par Pharmaceutical***

On October 22, 2004, we entered into a license and supply agreement granting Par Pharmaceutical the exclusive U.S. distribution and marketing rights to our generic calcitonin-salmon intranasal spray. Under the terms of the agreement with Par Pharmaceutical, we will obtain FDA approval, manufacture and supply finished generic calcitonin-salmon intranasal spray product to Par Pharmaceutical. Par Pharmaceutical will distribute the product in the United States. The financial terms of the agreement include milestone payments, product transfer payments for manufactured product and a profit sharing upon commercialization. Our ANDA filed with the FDA was accepted for review on February 17, 2004.

#### ***Questcor Pharmaceuticals, Inc.***

Under the terms of a supply agreement with Questcor Pharmaceuticals, Inc. ("Questcor"), subject to certain limitations, we are obligated to manufacture and supply all of Questcor's requirements and Questcor is obligated to purchase from us all of its requirements for the Nascobal® nasal gel and the Nascobal® nasal spray upon FDA's final approval. We have filed the New Drug Application ("NDA") and will continue to prosecute the pending U.S. patents for the Nascobal® nasal spray product on behalf of Questcor. In February 2005, Questcor paid a milestone fee of \$2.0 million upon final FDA approval of the NDA for the Nascobal® nasal spray, and has agreed to pay an additional \$2.0 million contingent upon issuance of a U.S. patent for the Nascobal® nasal spray.

#### ***Cytec Corporation***

In July 2003, we entered into an agreement with Cytec Corporation ("Cytec") pursuant to which Cytec acquired patent rights to our Mammary Aspirate Specimen Cytology Test ("MASCT") device. Under the terms of the agreement, we received a license fee from Cytec in 2003 and reimbursement for patent maintenance and further patent prosecution if incurred. We have the potential to receive additional milestone payments and royalties based on certain conditions.

## Business Strategy

Our goal is to become the leader in the development and commercialization of innovative, intranasal drug delivery products and technologies. Key elements of our strategy include:

- ***Applying Our Tight Junction Technology to Product Candidates and Other Drug Delivery Methods.*** We will focus our research and development efforts on product candidates where our proprietary intranasal drug delivery technology utilizing tight junctions will offer significant clinical advantages such as improved safety and clinical efficacy and increased patient compliance due to elimination of injection site pain and avoidance of injection site irritation. We will also continue to search for applications of our tight junction technology to improve other forms of drug delivery, including oral and intravenous delivery.
- ***Pursuing Collaborations with Leading Pharmaceutical and Biotechnology Companies.*** We will continue to establish strategic collaborations with leading pharmaceutical and biotechnology companies. Typically, we collaborate with partners to commercialize our product candidates by utilizing their research and development, regulatory compliance, marketing and distribution capabilities. We may also assist our collaboration partners in developing more effective drug delivery methods for their product candidates that have already completed early stage clinical trials. We intend to structure our collaborative arrangements to receive research and development funding and milestone payments during the development phase, revenue from manufacturing upon commercialization and royalties on future sales of products.
- ***Strategically Developing and Commercializing Product Candidates on Our Own.*** In select cases where we deem it to be strategically advantageous to us, we plan to internally develop, manufacture and distribute our products.
- ***Utilizing Our Manufacturing Expertise and Capabilities.*** We have invested substantial time and intellectual capital in developing our manufacturing facilities and know-how which we believe would be difficult for our competitors to replicate in the near term. These capabilities give us important competitive advantages including the ability to prepare the chemistry, manufacturing and controls section of the NDA filing with the FDA and maintain a high-level of quality control in manufacturing product candidates for clinical studies and FDA-approved products for commercialization. We are currently expanding our manufacturing capabilities in our Bothell, Washington facility which we believe will meet our projected capacity needs for the foreseeable future.

## Recent Developments

**Merck.** On September 24, 2004, we entered into an exclusive development, commercialization and license agreement and a separate exclusive supply agreement with Merck for the development and commercialization of PYY intranasal spray for the treatment of obesity. The collaborative arrangement provides that Merck will assume primary responsibility for conducting and funding pre-clinical and clinical studies and regulatory approvals, while we will be responsible for all manufacturing of PYY-related product. Merck will lead and fund world-wide commercialization, and we have the right to co-promote the product in the United States.

On January 26, 2005, we announced that Merck initiated a Phase I study for PYY intranasal spray for the treatment of obesity. This study being conducted by Merck builds upon our previous PYY clinical programs, under which 63 subjects have received more than 900 doses of intranasal PYY prior to Merck's initiation of this study.

**Questcor.** Under the terms of a supply agreement with Questcor, subject to certain limitations, we are obligated to manufacture and supply all of Questcor's requirements and Questcor is obligated to purchase from us all of its requirements for the Nascobal® nasal gel and the Nascobal® nasal spray upon FDA's final approval. We have filed the NDA and will continue to prosecute the pending U.S. patents for the Nascobal® nasal spray product on behalf of Questcor. In February 2005, Questcor paid a milestone fee of \$2.0 million upon final FDA approval of the NDA for

the Nascobal® nasal spray, and has agreed to pay an additional \$2.0 million contingent upon issuance of a U.S. patent for the Nascobal® nasal spray.

**Capital Raising.** On December 14, 2004, we completed a public offering of 4,250,000 shares of our common stock pursuant to our \$80 million effective shelf registration statement, with gross proceeds of approximately \$57.4 million to us, prior to the deduction of fees and commissions of \$4.5 million.

### **Manufacturing**

We plan to formulate, manufacture and package all of our products in two facilities. We have an FDA-approved 10,000 square foot commercial manufacturing facility in Hauppauge, New York with manufacturing capacity of approximately six million product units per year. In addition, we have a 20,000 square foot commercial manufacturing space contained within our corporate headquarters in Bothell, Washington. Upon completion of FDA review of our Bothell facility, our manufacturing capability of the combined facilities will be approximately 60 million product units per year.

The process for manufacturing our pharmaceutical products is technically complex, requires special skills and equipment and must be performed in a qualified facility in accordance with cGMP of the FDA. Our Hauppauge facility is capable of manufacturing products in quantities we believe are sufficient for clinical trials of product candidates as well as commercial supply sufficient to meet forecasted demand for at least the next two years.

We are expanding our commercial manufacturing facilities, in part, to meet anticipated manufacturing commitments for PYY intranasal spray contained in our supply agreement with Merck. There is sufficient room for further development of additional capacity at the Bothell facility that would increase our manufacturing capacity to accommodate additional products under development or to meet additional requirements under various supply agreements. We anticipate that full development of this site, including possible new construction on the surrounding property, can accommodate our space requirements for the foreseeable future. However, no assurance can be given that we will have the financial resources necessary to adequately expand our manufacturing capacity if and when the need arises.

Raw materials essential to our business are generally readily available from multiple sources. However, certain raw materials and components used to manufacture our products, including essential pharmaceutical ingredients and other critical components are available from limited sources. For example, our ANDA for generic calcitonin-salmon intranasal spray includes an active pharmaceutical compound supplied by one supplier. In addition, controlled substances including morphine gluconate are highly regulated by the U.S. Drug Enforcement Administration (the "DEA") and may be purchased only when a research and manufacturing license has been issued by the DEA to obtain these substances.

### **Sales and Marketing**

We plan to market our FDA approved products either on our own or through co-marketing, co-promotion, licensing or distribution arrangements with collaboration partners. We believe that our current approach allows us maximum flexibility in selecting the sales and marketing method that will both increase market penetration and commercial acceptance of our products and enable us to limit committing the considerable resources to develop a substantial sales and marketing organization. We currently have four personnel dedicated to business development and marketing and plan to hire additional staff as needed to support our growth.

### **Licenses, Patents and Proprietary Rights**

We intend to seek appropriate patent protection for our proprietary technologies by filing patent applications in the United States and certain foreign countries. As of February 15, 2005, we have 15 issued or allowed United States patents and 60 pending United States patent applications, including provisional patent applications. When

appropriate, we also seek foreign patent protection and to date have 26 issued or allowed foreign patents, and 101 pending foreign patent applications.

Our financial success will depend in large part on our ability to:

- obtain patent and other proprietary protection for our inventions;
- enforce and defend patents once obtained;
- operate without infringing the patents and proprietary rights of third parties; and
- preserve our trade secrets.

Our patents and patent applications are directed to composition of matter, methods of use and/or methods of manufacturing, as appropriate.

We apply for patents covering our discoveries and technologies as we deem appropriate. However, we may fail to apply for patents on important discoveries or technologies in a timely fashion or at all. Also, our pending patent applications may not result in the issuance of any patents. These applications may not be sufficient to meet the statutory requirements for patentability, and therefore we may be unable to obtain enforceable patents covering the related discoveries or technologies we may want to commercialize. In addition, because patent applications are maintained in secrecy for approximately 18 months after filing, other parties may have filed patent applications relating to inventions before our applications covering the same or similar inventions. In addition, foreign patent applications are often published initially in local languages, and until an English language translation is available it can be impossible to determine the significance of a third party invention. Any patent applications filed by third parties may prevail over our patent applications or may result in patents that issue alongside patents issued to us, leading to uncertainty over the scope of the patents or the freedom to practice the claimed inventions.

Although we have a number of issued patents, the discoveries or technologies covered by these patents may not have any therapeutic or commercial value. Also, issued patents may not provide commercially meaningful protection against competitors. Other parties may be able to design around our issued patents or independently develop products having effects similar or identical to our patented product candidates. In addition, the scope of our patents is subject to considerable uncertainty and competitors or other parties may obtain similar patents of uncertain scope.

## **Government Regulations**

Government authorities in the United States and other countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of drugs and biologic products. All of our product candidates are either drugs or biologic products, except for MASCT device, which is a medical device and is also extensively regulated.

In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug, and Cosmetic Act (the "FDCA") and implementing regulations thereunder, and other laws, including, in the case of biologics, the Public Health Service Act. Failure to comply with applicable U.S. requirements, both before and after approval, may subject us to administrative and judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecutions.

Before our drugs and biologic products may be marketed in the United States, each must be approved by the FDA. None of our product candidates, except for Nascobal® nasal gel and nasal spray, has received such approval. The steps required before a drug or a biologic product may be approved by FDA include pre-clinical laboratory and animal tests and formulation studies; submission to the FDA of an Investigational New Drug Exemption (an "IND")

for human clinical testing, which must become effective before human clinical trials may begin; adequate and well-controlled clinical trials to establish the safety and effectiveness of the product for each indication for which approval is sought; submission to the FDA of an NDA, in the case of a drug product, and a Biologics License Application (“BLA”), in the case of a biologic product; satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug or biologic product is produced to assess compliance with cGMP; and FDA review and approval of an NDA or BLA.

Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. There can be no assurance that submission of an IND will result in FDA authorization to commence clinical trials. Once an IND is in effect, each clinical study to be conducted under the IND must be submitted to the FDA, which may or may not allow the trial to proceed.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified physician-investigators and healthcare personnel. Clinical trials are conducted under protocols detailing, for example, the parameters to be used in monitoring patient safety and the safety and effectiveness criteria, or end points, to be evaluated. Clinical trials are typically conducted in three defined phases, but the phases may overlap or be combined. Each trial must be reviewed and approved by an independent Institutional Review Board before it can begin. Phase I usually involves the initial administration of the investigational drug or biologic product to people, usually normal volunteers, to evaluate its safety, dosage tolerance, pharmacodynamics and, if possible, to gain an early indication of its effectiveness. Phase II usually involves trials in a limited patient population, with the disease or condition for which the test material is being developed, to evaluate dosage tolerance and appropriate dosage; identify possible adverse side effects and safety risks; and preliminarily evaluate the effectiveness of the drug or biologic for specific indications. Phase III trials are designed to obtain the safety and efficacy data needed to create the package insert that accompanies the product upon commercialization, and are conducted by administering the drug or biologic candidate in its final form in an expanded patient population. We cannot be sure that Phase I, Phase II or Phase III clinical trials will be completed successfully within any specified period of time, if at all. Further, we, our product development partners, or the FDA may suspend clinical trials at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk or are obtaining no medical benefit from the test material.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and the clinical studies, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. Before approving an application, the FDA usually will inspect the facility(ies) at which the product is manufactured, and will not approve the product unless cGMP compliance is satisfactory. If the FDA determines the NDA or BLA is not acceptable, the FDA may outline the deficiencies in the NDA or BLA and often will request additional information. Notwithstanding the submission of any requested additional testing or information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Post-approval marketing of products in larger patient populations than were studied during development can lead to new findings about the safety or efficacy of the products. This information can lead to a product sponsor and/or the FDA requiring changes in the labeling of the product or even the withdrawal of the product from the market. The testing and approval process requires substantial time, effort and financial resources, and we cannot be sure that any approval will be granted on a timely basis, if at all.

Some of our product candidates may be eligible for submission of applications for approval that require less information than the NDAs described above. The FDA may approve an ANDA if the product is the same in

important respects as a listed drug, such as a drug with an effective FDA approval, or the FDA has declared it suitable for an ANDA submission. ANDAs for such generic drugs must generally contain the same manufacturing and composition information as NDAs, but applicants do not need to submit preclinical and often do not need to submit clinical safety and effectiveness data. Instead they must submit studies showing that the product is bioequivalent to the listed drug. Drugs are bioequivalent if the rate and extent of absorption of the drug does not show a significant difference from the rate and extent of absorption of the listed drug. Conducting bioequivalence studies is generally less time-consuming and costly than conducting pre-clinical and clinical studies necessary to support an NDA. We have submitted an ANDA for calcitonin that is currently pending before the FDA, and we may be able to submit ANDAs for other product candidates in the future.

The FDCA provides that ANDA reviews and/or approvals will be delayed in various circumstances. For example, the holder of the NDA for the listed drug may be entitled to a period of market exclusivity, during which FDA will not approve, and may not even review, the ANDA. If the listed drug is claimed by an unexpired patent that the NDA holder has listed with the FDA, the ANDA applicant must certify in a so-called paragraph IV certification that the patent is invalid, unenforceable, or not infringed by the product that is the subject of the ANDA. If the holder of the NDA sues the ANDA applicant within 45 days of being notified of the paragraph IV certification, the FDA will not approve the ANDA until the earlier of a court decision favorable to the ANDA applicant or the expiration of 30 months. Also, in circumstances in which the listed drug is claimed in an unexpired listed patent and the patent's validity, enforceability or applicability to the generic drug has been challenged by more than one generic applicant, ANDA approvals of later generic drugs may be delayed until the first applicant has received a 180-day period of market exclusivity. The regulations governing marketing exclusivity and patent protection are complex, and it is often unclear how they will be applied in particular circumstances until FDA acts on one or more ANDA applications. We do not believe that there is market exclusivity associated with the listed version of calcitonin and we have not been sued by the patent holder in connection with our ANDA for calcitonin, but our ANDA approval could be delayed by exclusivity awarded to a previous ANDA applicant.

Some of our drug products may be eligible for approval under the Section 505(b)(2) approval process. Section 505(b)(2) applications may be submitted for drug products that represent a modification of a listed drug (e.g., a new indication or new dosage form) and for which investigations other than bioavailability or bioequivalence studies are essential to the drug's approval. Section 505(b)(2) applications may rely on safety and effectiveness information submitted for the listed drug as well as information obtained by the 505(b)(2) applicant needed to support the modification of the listed drug. Preparing Section 505(b)(2) applications is also generally less costly and time-consuming than preparing an NDA. Like ANDAs, approval of Section 505(b)(2) applications may be delayed because of market exclusivity awarded to the listed drug or because patent rights are being adjudicated.

In addition, regardless of the type of approval, we and our partners are required to comply with a number of FDA requirements both before and after approval. For example, we are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotion for our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in all areas of regulatory compliance, including production and quality control to comply with cGMP. In addition, discovery of problems such as safety problems may result in changes in labeling or restrictions on a product manufacturer or NDA/BLA holder, including removal of the product from the market.

Our MASCT device that we have licensed to Cytyc is a medical device that requires FDA authorization before it may be marketed. Medical devices may be marketed pursuant to an approved Pre-Market Approval Application ("PMA"), or pursuant to a clearance under Section 510(k) of the FDCA. Obtaining a PMA involves generally the same steps as obtaining an NDA or BLA. Obtaining a 510(k) generally, but not always, requires the submission of less, but still substantial, performance, manufacturing, and other information. The MASCT device has been cleared for marketing under Section 510(k). In addition, medical devices are subject to pre- and post-approval and clearance requirements similar to those that apply to drugs and biologics.



In addition, we, our collaboration partners, and some of our product candidates, including our morphine gluconate and abuse-resistant opioid, are subject to the requirements of the Controlled Substances Act and implementing regulations thereunder, which are administered by the DEA. Establishments may not handle controlled drug substances until they have been inspected and registered by the DEA. The DEA also imposes recordkeeping and reporting requirements, procurement and manufacturing quotas, sales restrictions, and other obligations. Facilities must be equipped to meet DEA security requirements. We currently hold a DEA registration to conduct research at our Hauppauge facility relating to drug formulations containing DEA Schedule II controlled substances. However, there can be no assurance that we will be able to maintain our DEA registration or that we will be able to obtain additional registrations required to continue to research or commercially distribute our product candidates.

## **Competition**

Competition in the drug industry is intense. Although we are not aware of any other companies that have the scope of proprietary technologies and processes that we have developed in our ability to deliver both small and large molecule drugs by intranasal administration, there are a number of competitors who possess capabilities relevant to the drug delivery field. In particular, we face substantial competition from companies pursuing the commercialization of products using intranasal drug delivery technology such as Archimedes Pharma (“Archimedes”) (formerly West Pharmaceuticals Services, Inc.), Intranasal Technology, Inc. (“Intranasal Technology”), and Innovative Drug Delivery Systems, Inc. (“IDDS”). Established pharmaceutical companies such as AstraZeneca plc (“AstraZeneca”) and GlaxoSmithKline plc (“GlaxoSmithKline”) also have in-house intranasal drug delivery research and development programs that have successfully developed and are marketing products using intranasal drug delivery technology. We also face indirect competition from other companies with expertise in alternate drug delivery technologies such as oral, injectable, patch-based and pulmonary administration. These competitors include Alza Corporation, a Johnson & Johnson company (“Alza”), Alkermes, Inc. (“Alkermes”), Nektar Therapeutics, Inc. (“Nektar”), Skye Pharma plc (“Skye Pharma”), and Penwest Pharmaceuticals Co. (“Penwest Pharmaceuticals”). Many of our competitors have substantially greater capital resources, research and development resources and experience, manufacturing capabilities, regulatory expertise, sales and marketing resources, and established collaborative relationships with pharmaceutical companies. Our competitors, either alone or with their collaboration partners, may succeed in developing drug delivery technologies that are similar or preferable in effectiveness, safety, cost and ease of commercialization, and our competitors may obtain intellectual property protection or commercialize such products sooner than we do.

Universities and public and private research institutions are also potential competitors. While these organizations primarily have educational objectives, they may develop proprietary technologies related to the drug delivery field or secure protection that we may need for development of our technologies and products. We may attempt to license these proprietary technologies, but these licenses may not be available to us on acceptable terms, if at all.

Even if we are able to develop products and then obtain the necessary regulatory approvals, our success depends to a significant degree on the commercial success of products manufactured by us pursuant to supply agreements or distributed by our collaboration partners. If our product candidates obtain the necessary regulatory approvals and become commercialized, they would compete with the following products already in the market or currently in development stage:

### ***Obesity***

There are currently three products approved by the FDA for the treatment of obesity, Xenical (orlistat) by F. Hoffman-La Roche Ltd., Meridia (sibutramine) by Abbott Laboratories and the generic phentermine. In addition, there are other products currently in development for the treatment of obesity, including Acomplia (rimonabant) by Sanofi-SA, injectable PYY by Amylin Pharmaceuticals, Inc. and oral PYY by Emisphere Technologies, Inc. (“Emisphere Technologies”).

### ***Osteoporosis***

Pharmaceutical treatments for osteoporosis include bisphosphonates such as Merck's Fosamax (alendronate) and The Procter & Gamble Company/Aventis' Actonel (risedronate) and selective estrogen receptor modulators such as Eli Lilly's Evista (raloxifene). If commercialized, our intranasal PTH<sub>(1-34)</sub> will also compete directly with Eli Lilly's Forteo (teriparatide), an FDA approved injectable parathyroid hormone. Additional competition could come from development candidates such as injectable full length parathyroid hormone by NPS Pharmaceuticals, Inc. Our generic calcitonin-salmon intranasal spray to be manufactured by us and distributed by Par Pharmaceutical will compete with Novartis' Miacalcin (intranasal calcitonin-salmon). Novartis may introduce an authorized generic version through Sandoz US, its wholly-owned subsidiary and Apotex has filed a generic application of intranasal salmon-calcitonin. Additional competition could come from development candidates such as oral calcitonin by Emisphere Technologies and recombinant salmon-calcitonin from Unigene, Inc.

### ***Erectile Dysfunction***

There are three PDE-5 inhibitors approved by the FDA, Viagra (sildenafil) by Pfizer, Cialis (tadalafil) by Eli Lilly/ICOS and Levitra (vardenafil) by Bayer Pharmaceuticals Corporation, GlaxoSmithKline and Schering Corporation, as well as Uprima (sublingual apomorphine) by TAP Pharmaceutical Products, Inc. marketed in Europe. In addition, products such as Palatin's PT-141 intranasal spray are also in development for treatment of erectile dysfunction.

### ***Breakthrough Cancer Pain***

Currently, the only approved pharmaceutical treatment for breakthrough cancer pain is Actiq (oral transmucosal fentanyl citrate) by Cephalon. In addition, OraVescent (a quick dissolve formulation of fentanyl) by Cephalon is also in development.

### ***Multiple Sclerosis***

Pharmaceutical treatments for multiple sclerosis include Rebif by Serono/Pfizer, Avonex and Tysabri, formerly Antegren (natalizumab), by Biogen Idec Inc., Betaseron by Berlex Biosciences ("Berlex")/Chiron, and Copaxone by Teva Pharmaceutical Industries Ltd. Additional competition could come from development candidates such as NBI-5788 (an altered peptide ligand) being developed by Neurocrine Biosciences, Inc.

### **Product Liability**

Testing, manufacturing and marketing products involve an inherent risk of product liability attributable to unwanted and potentially serious health effects. To the extent we elect to test, manufacture or market products independently, we will bear the risk of product liability directly. We currently have product liability insurance coverage in the amount of \$10 million per occurrence and a \$20 million aggregate limitation, subject to a deductible of \$10,000 per occurrence.

### **Employees**

We had 106 full-time employees at January 31, 2005, 78 of whom are engaged in research and development, and the others are engaged in administration and support functions. None of our employees is covered by a collective bargaining agreement.

### **RISK FACTORS**

You should carefully consider the risks described below before making an investment decision.

**We do not generate operating income and will require additional financing in the future. If additional capital is not available, we may have to curtail or cease operations.**

Our business currently does not generate the cash that is necessary to finance our operations. We incurred losses from operations (excluding interest income/expense and other income/expense) of \$13.6 million in 2002, \$6.2 million in 2003 and \$28.5 million in 2004. Subject to the success of our development programs and potential licensing transactions, we will need to raise additional capital to fund research and development, to develop and commercialize our product candidates, to enhance existing services, to respond to competitive pressures and to acquire complementary businesses or technologies. Our future capital needs depend on many factors, including:

- the scope, duration and expenditures associated with our research and development programs;
- continued scientific progress in these programs;
- the outcome of potential licensing transactions, if any;
- competing technological developments;
- our proprietary patent position, if any, in our products; and
- the regulatory approval process for our products.

We may seek to raise necessary funds through public or private equity offerings, debt financings or additional strategic alliances and licensing arrangements. We may not be able to obtain additional financing on terms favorable to us, if at all. General market conditions may make it very difficult for us to seek financing from the capital markets. We may be required to relinquish rights to our technologies or drug candidates, or grant licenses on terms that are not favorable to us in order to raise additional funds through alliance, joint venture or licensing arrangements. If adequate funds are not available, we may have to delay, reduce or eliminate one or more of our research or development programs and reduce overall overhead expenses. These actions would likely reduce the market price of our common stock. See "Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources - Liquidity."

**We have not been profitable on an annual basis for eight years, and we may never become profitable.**

We have incurred net losses in each of the past eight years. As of December 31, 2004, we had an accumulated deficit of approximately \$83.5 million and expect additional operating losses in the foreseeable future as we continue our research and development activities.

The process of developing our products requires significant research and development efforts, including basic research, preclinical and clinical development, as well as FDA regulatory approval. These activities, together with our sales, marketing, general and administrative expenses, have resulted in operating losses in the past, and there can be no assurance that we can achieve profitability in the future. Our ability to achieve profitability depends on our ability, alone or with our collaborators, to develop our drug candidates, conduct clinical trials, obtain necessary regulatory approvals, and manufacture, distribute, market and sell our drug products. We cannot assure you that we will be successful at any of these activities or predict when we will ever become profitable.

**We are dependent on our collaborative arrangements with third parties for a substantial portion of our revenue, and our development and commercialization activities may be delayed or reduced if we fail to negotiate or maintain successful collaborative arrangements.**

We are dependent on our current and any other possible future collaborators to commercialize many of our product candidates and to provide the regulatory compliance, sales, marketing and distribution capabilities required for the success of our business. If we fail to secure or maintain successful collaborative arrangements, our

development and commercialization activities will be delayed or reduced and our revenues will be materially and adversely impacted.

We entered into new collaboration partnerships with Merck in September 2004 and Par Pharmaceutical in October 2004. Over the next several years, we will depend on these collaborative partnerships for a significant portion of our revenue. The expected future milestone payments and cost reimbursements under these collaborations will provide an important source of financing for our research and development program, thereby facilitating the application of our technology to the development of our PYY product and enabling the commercialization of our generic calcitonin-salmon intranasal spray, which may produce significant royalty revenue. These collaborative agreements can be terminated by our partners in their discretion upon the satisfaction of certain notice requirements. Our partners are not precluded from independently pursuing competing products and drug delivery approaches or technologies. Even if our partners continue their contributions to our collaborative arrangements, they may nevertheless determine not to actively pursue the development or commercialization of any resulting products. Our partners may fail to perform their obligations under the collaborative arrangements or may be slow in performing their obligations. In addition, our partners may experience financial difficulties at any time that could prevent them from having available funds to contribute to these collaborations. If our collaborating partners fail to conduct their commercialization, regulatory compliance, sales and marketing or distribution activities successfully and in a timely manner, we will earn little or no revenue from those products and we will not be able to achieve our objectives or build a sustainable or profitable business.

**Our success depends to a significant degree upon the commercial success of products manufactured by us pursuant to supply agreements or marketed by our collaborating partners.**

Even if we are able to develop products and obtain the necessary regulatory approvals, our success depends to a significant degree on the commercial success of products manufactured by us pursuant to supply agreements or marketed by our collaborating partners. If these products fail to achieve or subsequently maintain market acceptance or commercial viability, our business would be significantly harmed because our revenue is dependent upon sales of these products.

**Even if we are successful in commercializing a product candidate, it is possible that the commercial opportunity for intranasally-administered products will be limited.**

None of our product candidates utilizing our intranasal drug delivery technology have been brought to market. Accordingly, while we believe there is a commercial market for our intranasal drug delivery technology, there can be no assurance that our intranasal drug delivery technology will become a viable commercial alternative to other drug delivery methods. Many factors may affect the market acceptance and commercial success of any potential products, including:

- establishment and demonstration of the effectiveness and safety of the drugs;
- timing of market entry as compared to competitive products;
- the benefits of our drugs relative to their prices and the comparative price of competing products;
- actual and perceived benefits and detriments of intranasal drug delivery, which may be affected by press and academic literature;
- marketing and distribution support of our products; and
- any restrictions on labeled indications.

**Our revenues and profits from any particular generic pharmaceutical products decline as our competitors introduce their own generic equivalents.**

On October 22, 2004, we entered into a license and supply agreement granting Par Pharmaceutical the exclusive U.S. distribution and marketing rights to our generic calcitonin-salmon intranasal spray. Under the terms of the agreement with Par Pharmaceutical, we will obtain FDA approval, manufacture and supply finished generic calcitonin-salmon intranasal spray to Par Pharmaceutical. Par Pharmaceutical will distribute the product in the United States. Novartis, the supplier of branded calcitonin-salmon intranasal spray, may introduce a generic version through Sandoz US, its wholly-owned subsidiary. Selling prices of generic drugs typically decline, sometimes dramatically, as additional companies receive approvals for a given product and competition intensifies. To the extent that our collaborating partner and we succeed in being the first to market a generic version of a significant product, our initial sales and profitability following the introduction of such product will be subject to material reduction upon a competitor's introduction of the equivalent product. Our ability to sustain our sales and profitability on any product over time is dependent on both the number of new competitors for such product and the timing of their approvals.

**Clinical trials of our product candidates are expensive and time-consuming, and the results of these trials are uncertain.**

Many of our research and development programs are at an early stage. Clinical trials in patients are long, expensive and uncertain processes. The length of time generally varies substantially according to the type of drug, complexity of clinical trial design, regulatory compliance requirements, intended use of the drug candidate and rate of patient enrollment for the clinical trials. Clinical trials may not be commenced or completed on schedule, and the FDA may not ultimately approve our product candidates for commercial sale. Further, even if the results of our preclinical studies or clinical trials are initially positive, it is possible that we will obtain different results in the later stages of drug development or that results seen in clinical trials will not continue with longer term treatment. Drugs in late stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. For example, positive results in early Phase I or Phase II clinical trials may not be repeated in larger Phase II or Phase III clinical trials. All of our potential drug candidates are prone to the risks of failure inherent in drug development. The clinical trials of any or all of our drug candidates, including apomorphine HCl intranasal spray, generic calcitonin-salmon intranasal spray, beta interferon, morphine gluconate, oral abuse-resistant opioid, PTH<sub>(1-34)</sub> and PYY intranasal spray could be unsuccessful, which would prevent us from commercializing these drugs. The FDA conducts its own independent analysis of some or all of the pre-clinical and clinical study data submitted in a regulatory filing and often comes to different and potentially more negative conclusions than the analysis performed by the drug sponsor. Our failure to develop safe, commercially viable drugs approved by the FDA would substantially impair our ability to generate revenues and sustain our operations and would materially harm our business and adversely affect our stock price. In addition, significant delays in clinical trials will impede our ability to seek regulatory approvals, commercialize our drug candidates and generate revenue, as well as substantially increase our development costs.

**We are subject to extensive government regulation including the requirement of approval before our products may be marketed.**

We, our collaboration partners, and our product candidates are subject to extensive regulation by governmental authorities in the U.S. and other countries. Failure to comply with applicable requirements could result in, among other things, any of the following actions: warning letters; fines and other civil penalties; unanticipated expenditures; delays in approving or refusal to approve a product candidate; product recall or seizure; interruption of manufacturing or clinical trials; operating restrictions; injunctions; and criminal prosecution.

Our product candidates cannot be marketed in the United States without FDA approval or clearance. The FDA has approved only two of our product candidates, Nascobal® nasal gel and Nascobal® nasal spray, and cleared only one, our MASCT device, for sale in the United States. Our other product candidates are in development, and will have to be approved by the FDA before they can be marketed in the United States. Obtaining FDA approval requires

substantial time, effort, and financial resources, and there can be no assurance that any approval will be granted on a timely basis, if at all. If the FDA does not approve our product candidates in a timely fashion, or does not approve them at all, our business and financial condition may be adversely affected. We, our collaboration partners, or the FDA may suspend or terminate human clinical trials at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

In addition, both before and after regulatory approval, we, our collaboration partners, and our product candidates are subject to numerous FDA requirements covering, among other things, testing, manufacturing, quality control, labeling, advertising, promotion, distribution, and export. The FDA's requirements may change and additional government regulations may be promulgated that could affect us, our collaboration partners, and our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. There can be no assurance that we will not be required to incur significant costs to comply with such laws and regulations in the future or that such laws or regulations will not have a material adverse effect upon our business.

In addition, some of our product candidates, including our morphine gluconate and abuse-resistant opioid, will be subject to the requirements of the Controlled Substances Act and implementing regulations thereunder, which are administered by the DEA. Establishments may not handle controlled drug substances until they have been inspected and registered by the DEA. The DEA also imposes recordkeeping and reporting requirements, procurement and manufacturing quotas, sales restrictions, and other obligations. Facilities must be equipped to meet DEA security requirements. We currently hold a DEA registration to conduct research at our Hauppauge facility relating to drug formulations containing DEA Schedule II controlled substances. However, there can be no assurance that we will be able to maintain our DEA registration or that we will be able to obtain additional registrations required to continue to research or commercially distribute our product candidates.

**Our operating results are subject to significant fluctuations and uncertainties, and our failure to meet expectations of public market analysts or investors regarding operating results may cause our stock price to decline.**

Our operating results are subject to significant fluctuations and uncertainties due to a number of factors including, among others:

- timing and achievement of licensing transactions, including milestones and other performance factors associated with these contracts;
- time and costs involved in patent prosecution and development of our proprietary position;
- continued scientific progress and level of expenditures in our research and development programs;
- cost of manufacturing scale-up and production batches, including vendor provided activities and costs;
- time and costs involved in obtaining regulatory approvals;
- changes in general economic conditions and drug delivery technologies;
- expiration of existing patents and related revenues; and
- new products and product enhancements that we or our competitors introduce.

As a result of these factors and other uncertainties, our operating results have fluctuated significantly in recent years, resulting in net losses of \$13.5 million in 2002, \$2.1 million in 2003 and \$28.6 million in 2004.

Our revenues and operating results, particularly those reported on a quarterly basis, will continue to fluctuate significantly. This fluctuation makes it difficult to forecast our operating results. Therefore, we believe that quarterly comparisons of our operating results may not be meaningful, and you should not rely on them as an indication of our future performance. In addition, our operating results in a future quarter or quarters may fall below the expectations of public market analysts or investors. If this were to occur, the price of our stock could decline.

**If we are unable to adequately protect our proprietary technology from legal challenges, infringement or alternative technologies, this inability will hurt our competitive position and negatively impact our operating results.**

We specialize in the intranasal delivery of pharmaceutical products and rely on the issuance of patents, both in the United States and internationally, for protection against competitive drug delivery technologies. Although we believe that we exercise the necessary due diligence in our patent filings, our proprietary position is not established until the appropriate regulatory authorities actually issue a patent, which may take over three years from initial filing or may never occur. As of February 15, 2005, we have 41 patents issued and 161 patent applications filed.

Moreover, even the established patent positions of pharmaceutical companies are generally uncertain and involve complex legal and factual issues. Although we believe our issued patents are valid, third parties may infringe our patents or may initiate proceedings challenging the validity or enforceability of our patents. The issuance of a patent is not conclusive as to its claim scope, validity or enforceability. Challenges raised in patent infringement litigation we initiate or in proceedings initiated by third parties may result in determinations that our patents have not been infringed or that they are invalid, unenforceable or otherwise subject to limitations. In the event of any such determinations, third parties may be able to use the discoveries or technologies claimed in our patents without paying licensing fees or royalties to us, which could significantly diminish the value of these discoveries or technologies. As a result of such determinations, we may be enjoined from pursuing research, development or commercialization of potential products or may be required to obtain licenses, if available, to the third party patents or to develop or obtain alternative technology. Responding to challenges initiated by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns.

Furthermore, it is possible that others will infringe or otherwise circumvent our issued patents and that we will be unable to fund the cost of litigation against them or elect not to pursue litigation. In addition, enforcing our patents against third parties may require significant expenditures regardless of the outcome of such efforts. We also cannot assure you that others have not filed patent applications for technology covered by our pending applications or that we were the first to invent the technology. There may also exist third party patents or patent applications relevant to our potential products that may block or compete with the technologies covered by our patent applications and third parties may independently develop intellectual property similar to our patented intellectual property, which could result in, among other things, interference proceedings in the United States Patent and Trademark Office to determine priority of invention.

In addition, we may not be able to protect our established and pending patent positions from competitive drug delivery technologies, which may provide more effective therapeutic benefit to patients and which may therefore make our products, technology and proprietary position obsolete.

If we are unable to adequately protect our proprietary technology from legal challenges, infringement or alternative technologies, we will not be able to compete effectively in the pharmaceutical delivery business.

**Because intellectual property rights are of limited duration, expiration of intellectual property rights and licenses will negatively impact our operating results.**

Intellectual property rights, such as patents and license agreements based on those patents, generally are of limited duration. Our operating results depend on our patents and intellectual property licenses. Therefore, the

expiration or other loss of rights associated with intellectual property and intellectual property licenses can negatively impact our business.

**Our product development efforts may not result in commercial products.**

Our future results of operations depend, to a significant degree, upon our and our collaborating partners' ability to successfully commercialize additional pharmaceutical products. The development and commercialization process, particularly with respect to innovative products, is both time consuming and costly and involves a high degree of business risk. Successful product development in the pharmaceutical industry is highly uncertain, and very few research and development projects result in a commercial product. Product candidates that appear promising in the early phases of development, such as in early human clinical trials, may fail to reach the market for a number of reasons, such as:

- product candidates may not perform as expected in later or broader trials in humans and limit marketability of such product candidate;
- necessary regulatory approvals may not be obtained in a timely manner, if at all;
- product candidates may not be able to be successfully and profitably produced and marketed;
- third parties have proprietary rights to a product candidate, and do not allow sale on reasonable terms;
- product candidate may not be financially successful because of existing therapeutics that offer equivalent or better treatments; or
- suppliers of product pumps or actuators required to atomize our formulations may increase their price or cease to manufacture them without prior notice.

To date, none of the product candidates utilizing our current intranasal drug delivery technology have been approved by the FDA. Accordingly, there can be no assurance that any of our product candidates currently in development will ever be successfully commercialized, and delays in any part of the process or our inability to obtain regulatory approval could adversely affect our operating results by restricting introduction of new products by us or our collaborating partners.

**We have limited experience in marketing or selling our products, and we may need to rely on marketing partners or contract sales companies.**

Even if we are able to develop our products and obtain necessary regulatory approvals, we have limited experience or capabilities in marketing or commercializing our products. We currently have a limited sales, marketing or distribution infrastructure. Accordingly, we are dependent on our ability to find collaborative marketing partners or contract sales companies for commercial sale of our internally-developed products. Even if we find a potential marketing partner, we may not be able to negotiate a licensing contract on favorable terms to justify our investment or achieve adequate revenues.

**Coverage and reimbursement status of newly approved drugs is uncertain and the failure to obtain adequate reimbursement coverage could limit our ability to generate revenue.**

Our products may prove to be unsuccessful if various parties, including government health administration authorities, private healthcare insurers and other healthcare payers, such as health maintenance organizations and self-insured employee plans that determine reimbursement to the consumer, do not accept our products for reimbursement. Sales of therapeutic and other pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from these third party payers. Third party payers are increasingly challenging the prices charged for medical products and services. We cannot assure you that reimbursement will be available at all



or at levels sufficient to allow our marketing partners to achieve profitable price levels for our products. If we fail to achieve adequate reimbursement levels, patients may not purchase our products and sales of these products will be absent or reduced.

**We may be required to defend lawsuits or pay damages for product liability claims.**

Our business inherently exposes us to potential product liability claims. We face substantial product liability exposure in human clinical trials and for products that we sell, or manufacture for others to sell, after regulatory approval. The risk exists even with respect to those drugs that are approved by regulatory agencies for commercial distribution and sale and manufactured in facilities licensed and regulated by regulatory agencies. Product liability claims, regardless of their merits, could be costly and divert management's attention, and adversely affect our reputation and the demand for our products.

We currently have product liability insurance coverage in the amount of \$10 million per occurrence and a \$20 million aggregate limitation, subject to a deductible of \$10,000 per occurrence. From time to time, the pharmaceutical industry has experienced difficulty in obtaining product liability insurance coverage for certain products or coverage in the desired amounts or with the desired deductibles. We cannot assure you that we will be able to obtain the levels or types of insurance we would otherwise have obtained prior to these market changes or that the insurance coverage we do obtain will not contain large deductibles or fail to cover certain liabilities or that it will otherwise cover all potential losses.

**We may be unable to compete successfully against our current and future competitors.**

Competition in the drug delivery industry is intense. In particular, we face substantial competition from companies pursuing the commercialization of products using intranasal drug delivery technology such as Archimedes, Intranasal Technology and IDDS. Established pharmaceutical companies such as AstraZeneca and GlaxoSmithKline also have in-house intranasal drug delivery research and development programs that have successfully developed and are marketing products using intranasal drug delivery technology. We also face indirect competition from other companies with expertise in alternate drug delivery technologies such as oral, injectable, patch-based and pulmonary administration. These competitors include Alza, Alkermes, Nektar, Skye Pharma and Penwest Pharmaceuticals.

Universities and public and private research institutions are also potential competitors. While these organizations primarily have educational objectives, they may develop proprietary technologies related to the drug delivery field or secure protection that we may need for development of our technologies and products. We may attempt to license these proprietary technologies, but these licenses may not be available to us on acceptable terms, if at all.

Many of our competitors have substantially greater capital resources, research and development resources and experience, manufacturing capabilities, regulatory expertise, sales and marketing resources, and established collaborating relationships with pharmaceutical companies. Our competitors, either alone or with their collaboration partners, may succeed in developing drug delivery technologies that are similar or preferable in effectiveness, safety, cost and ease of commercialization, and our competitors may obtain intellectual property protection or commercialize such products sooner than we do. Developments by others may render our product candidates or our technologies obsolete or, if developed earlier than our products, may achieve market acceptance which could negatively impact the opportunities for our products regardless of the merits of our technology.

**If we have a problem with our manufacturing facilities, we may not be able to market our products or conduct clinical trials.**

A substantial portion of our products for both clinical and commercial use is currently manufactured at our facility in Hauppauge, New York, and we are currently customizing our facility in Bothell, Washington to enable large-scale manufacturing. Our manufacturing capacity of the New York facility is approximately 6 million product units per year, and our manufacturing capacity of the Washington facility will be approximately 54 million product

units per year upon completion of FDA review which is anticipated in 2005. If we have a problem at either of our manufacturing facilities, it could cause a delay in clinical trials or the supply of product to market. Any significant delay or failure to manufacture could jeopardize our performance contracts with collaboration partners, resulting in material penalties to us and jeopardizing the commercial viability of our products.

**We use hazardous chemicals and radioactive and biological materials in our business. Any disputes relating to improper use, handling, storage or disposal of these materials could be time-consuming and costly.**

Our research and development operations involve the use of hazardous, radioactive and biological, potentially infectious, materials. We are subject to the risk of accidental contamination or discharge or any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to damages, fines and penalties in the event of an improper or unauthorized release of, or exposure of individuals to, these hazardous materials, and our liability could exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our business.

**Reforms in the healthcare industry and the uncertainty associated with pharmaceutical pricing, reimbursement and related matters could adversely affect the marketing, pricing and demand for our products.**

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the United States healthcare system have been introduced or proposed in Congress and in some state legislatures, including reductions in the cost of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products. For example, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 and the proposed rules thereunder impose new requirements for the distribution and pricing of prescription drugs in 2004, which could reduce reimbursement of prescription drugs for healthcare providers and insurers. Although we cannot predict the full effect on our business of the implementation of this legislation, we believe that legislation that reduces reimbursement for our products could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our products. This could materially and adversely impact our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of our products, which may adversely impact product sales.

**If we lose our key personnel, or if we are unable to attract and retain additional personnel, then we may be unable to successfully develop our business.**

If we are unable to retain one or more of our corporate officers, Dr. Steven C. Quay, Chairman of the Board, President and Chief Executive Officer, Dr. Gordon C. Brandt, Executive Vice President Clinical Research and Medical Affairs, Dr. Paul H. Johnson, Senior Vice President, Research and Development and Chief Scientific Officer, Gregory L. Weaver, CPA, MBA, Chief Financial Officer and Corporate Secretary, David E. Wormuth, Senior Vice President, Operations, Timothy M. Duffy, Vice President, Marketing and Business Development, or any of our other key managers or key technical personnel, our business could be seriously harmed. Except for the employment agreements with Dr. Quay and Mr. Weaver, we generally do not execute employment agreements with members of our management team. Whether or not a member of management has executed an employment agreement, there can be no assurance that we will be able to retain our key managers or key technical personnel or replace any of them if we lose their services for any reason. We make a significant effort and allocate substantial resources to recruit candidates to our Washington state and New York offices that are each located a significant distance away from many pharmaceutical and biotechnology companies. Competition for competent managers and technical personnel is intense, and failure to retain our key personnel may:

- compromise our ability to negotiate and enter into additional collaborative arrangements;

- delay our ongoing discovery research efforts;
- delay preclinical or clinical testing of our product candidates;
- delay the regulatory approval process; or
- prevent us from successfully commercializing our product candidates.

In addition, if we have to replace any of these individuals, we will not be able to replace knowledge that they have about our operations.

**We may encounter difficulties managing our growth, which could adversely affect our business.**

We increased the number of our full-time employees from 52 on December 31, 2002 to 106 on January 31, 2005, and we expect to continue to grow to meet our strategic objectives. If our growth continues, it may place a strain on us, our management and our resources. Our ability to effectively manage our operations, growth and various projects requires us to continue to improve our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. We may not be able to successfully implement these tasks on a larger scale and, accordingly, we may not achieve our research, development and commercialization goals. If we fail to improve our operational, financial and management information systems, or fail to effectively monitor or manage our new and future employees or our growth, our business could suffer significantly. In addition, no assurance can be made that we will be able to secure adequate facilities to house our staff, conduct our research or achieve our business objectives.

**We cannot assure you that our stock price will not decline.**

The market price of our common stock could be subject to significant fluctuations. Among the factors that could affect our stock price are:

- negative results from our clinical or pre-clinical studies or adverse FDA decisions related to our product candidates or third party products that are in the same drug class as our products;
- changes in revenue estimates or publication of research reports by analysts or the decision of analysts to drop coverage of us;
- failure to meet analysts' revenue estimates;
- speculation in the press or investment community;
- strategic actions by us or our competitors, such as acquisitions or restructurings;
- actions by institutional stockholders, hedge funds and significant stockholders of us;
- low average daily trading volumes due to relatively small number of shares outstanding;
- general market conditions; and
- domestic and international economic factors unrelated to our performance.

Additionally, numerous factors relating to our business may cause fluctuations or declines in our stock price.

The stock markets in general and the markets for pharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock.

**A significant number of shares of our common stock are subject to options and warrants, and we expect to sell additional shares of our common stock in the future. Sales of these shares will dilute the interests of other security holders and may depress the price of our common stock.**

As of December 31, 2004, there were 17,895,976 shares of common stock outstanding. As of such date, there were vested outstanding options to purchase 1,893,567 shares of common stock, unvested outstanding options to purchase 865,685 shares of common stock and outstanding warrants to purchase 1,486,073 shares of common stock. In addition, we may issue additional common stock and warrants from time to time to finance our operations. For example, we completed a public offering of 4,250,000 shares of our common stock on December 14, 2004 and a private placement of 1,136,364 shares of our common stock in June 2004 to raise capital for general corporate purposes.

We may also issue additional shares to fund potential acquisitions or in connection with additional stock options or restricted stock granted to our employees, officers, directors and consultants under our stock option plans. The issuance, perception that issuance may occur, or exercise of warrants or options will have a dilutive impact on other stockholders and could have a material negative effect on the market price of our common stock.

**We have never paid cash or stock dividends on our common stock and we do not anticipate paying dividends in the foreseeable future.**

We have paid no cash or stock dividends on any of our classes of common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. The terms of our current borrowing facility prohibit the payment of dividends without bank approval. In addition, the terms of any future debt or credit facility may preclude us from paying any dividends. As a result, capital appreciation, if any, of our common stock may be the sole source of potential gain for the foreseeable future.

**The anti-takeover provisions of our stockholder rights plan may entrench management, may delay or prevent beneficial takeover bids by third parties and may prevent or frustrate any stockholder attempt to replace or remove the current management even if the stockholders consider it beneficial to do so.**

We have a stockholder rights plan designed to protect our stockholders from coercive or unfair takeover tactics. Under the plan, we declared a dividend of one preferred stock purchase right for each share of common stock outstanding on March 17, 2000. Each preferred stock purchase right entitles the holder to purchase from us 1/1000 of a share of Series A Junior Participating Preferred Stock for \$50. In the event any acquiring entity or group accumulates or initiates a tender offer to purchase 15% or more of our common stock, then each holder of a preferred stock purchase right, other than the acquiring entity and its affiliates, will have the right to receive, upon exercise of the preferred stock purchase right, shares of our common stock or shares in the acquiring entity having a value equal to two times the exercise price of the preferred stock purchase right.

The intent of the stockholder rights plan is to protect our stockholders' interests by encouraging anyone seeking control of our company to negotiate with our board of directors ("the Board"). However, our stockholder rights plan could make it more difficult for a third party to acquire us without the consent of the Board, even if doing so may be beneficial to our stockholders. This plan may discourage, delay or prevent a tender offer or takeover attempt, including offers or attempts that could result in a premium over the market price of our common stock. This plan could reduce the price that investors might be willing to pay for shares of our common stock in the future. Furthermore, the anti-takeover provisions of our stockholder rights plan may entrench management and make it more difficult for stockholders to replace management even if the stockholders consider it beneficial to do so.

**An interruption in the supply of our raw and bulk materials needed to make our products could cause our product development and commercialization to be slowed or stopped.**

We currently obtain supplies of critical raw and bulk materials used in our research and development and manufacturing efforts from several suppliers. However, we do not have long-term contracts with any of these suppliers. While our existing arrangements supply sufficient quantities of raw and bulk materials needed to accomplish the clinical development of our product candidates, there can be no assurance that we would have the capability to manufacture sufficient quantities of our product candidates to meet our needs if our suppliers are unable or unwilling to supply such materials. Any delay or disruption in the availability of raw or bulk materials could slow or stop product development and commercialization of the relevant product. Our dependence upon third parties for the manufacture of our bottles, pumps, and cap components of our intranasal products and the related supply chain may adversely affect our cost of goods, our ability to develop and commercialize products on a timely and competitive basis, and the production volume of our intranasal products.

### **Corporation Information**

We were incorporated in Delaware on September 23, 1983. Our principal executive offices are located at 3450 Monte Villa Parkway, Bothell, Washington 98021 and our telephone number is (425) 908-3600. We have an internet web address at <http://www.nastech.com>.

### **Available Information**

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission ("SEC"). The public may read and copy any documents each company files at the SEC's Public Reference Room at 450 Fifth Street N.W., Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. SEC filings are also available to the public from the SEC's Internet website at <http://www.sec.gov>.

We make available through our website at <http://www.nastech.com> our Annual Reports on Form 10-K or Form 10-K/A, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish such material to the SEC. In addition, our internet website includes other items related to corporate governance matters, including, among other things, charters of various committees of the Board and the code of business conduct and ethics applicable to all employees, officers and directors. Copies of these documents may be obtained, free of charge, from our internet website. Any shareholder also may obtain copies of these documents, free of charge, by sending a request in writing to: Nastech Pharmaceutical Company Inc., 3450 Monte Villa Parkway, Bothell, WA, 98021, Attn: Investor Relations.

## **ITEM 2. PROPERTIES**

We currently lease approximately 51,000 square feet of space at our corporate headquarters in Bothell, Washington. This includes approximately 14,000 square feet we leased effective January 1, 2005. Our Bothell facility consists of approximately 23,000 square feet of research and development facilities, approximately 20,000 square feet of manufacturing space and approximately 8,000 square feet of general and administrative space. The lease for our headquarters in Bothell expires in January 2016.

We also lease approximately 10,000 square feet of manufacturing space that we lease in Hauppauge, New York. This lease is scheduled to expire in June 2005, and we are currently negotiating to extend the Hauppauge lease for several years.

Future minimum lease payment obligations are approximately \$20.4 million. Annual lease expenses will be approximately \$1.8 million in 2005 and thereafter. We are also responsible for all utilities, maintenance, security and property tax increases related to our properties.

We believe that these facilities are adequate for our current needs, although we may in the future expand our facilities for additional research and development and manufacturing capability.

**ITEM 3. LEGAL PROCEEDINGS**

None.

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

There were no matters submitted to the vote of security holders through the solicitation of proxies or otherwise, during the last quarter of the fiscal period covered by this report.

## PART II

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

#### Market Information

Our common stock is listed on the Nasdaq National Market under the symbol "NSTK." The following table sets forth, for each of the quarterly periods indicated, the range of high and low sales prices of our common stock, as reported on the Nasdaq National Market.

Quarter	High	Low
2003:		
First Quarter.....	\$ 9.95	\$ 6.76
Second Quarter.....	11.95	7.06
Third Quarter.....	11.19	7.57
Fourth Quarter.....	10.70	8.30
2004:		
First Quarter.....	\$ 14.65	\$ 9.01
Second Quarter.....	14.95	9.40
Third Quarter.....	15.05	7.25
Fourth Quarter.....	16.56	11.95

On March 7, 2005, the closing price of our common stock reported on the Nasdaq National Market was \$9.71 per share.

As of February 15, 2005 there were approximately 9,400 beneficial holders of our common stock, including several brokerage firms holding shares in street name for beneficial owners.

#### Dividend Policy

We have never declared any cash dividends on our common stock. In addition, we have no current plans to pay any dividends on our common stock and intend to retain earnings, if any, for working capital purposes. The terms of our current credit facility prohibit the payment of dividends without bank approval. Any future decision to pay dividends on our common stock will depend upon our results of operations, capital requirements, our financial condition and other factors that the Board deems relevant.

#### Securities Authorized For Issuance Under Equity Compensation Plans

Information regarding securities authorized for issuance under our equity compensation plans is disclosed in Item 12: Security Ownership of Certain Beneficial Owners and Management.

#### Unregistered Sales of Equity Securities

(1) *Warrants.* During the three months ended December 31, 2004:

(i) the Company issued 65,900 shares of common stock to four holders of common stock warrants (the "Warrants") upon the exercise of such Warrants in private offerings pursuant to Section 4(2) of the Securities Act. The holders of the Warrants were accredited investors under Rule 501 of the Securities Act. The Company has registered the resale of such shares under the Securities Act. The Warrants were exercisable for an equal number of shares of common stock at an exercise price of \$7.50 per share, and;

(ii) the Company issued 8,832 shares of common stock to two holders of Warrants upon the cashless exercise of the Warrants to purchase 48,143 shares of common stock in private offerings pursuant to Section

4(2) of the Securities Act. The holders of the Warrants were accredited investors under Rule 501 of the Securities Act. The Company has registered the resale of such shares under the Securities Act. The Warrants were exercisable for an equal number of shares of common stock at an exercise price of \$11.09 per share. The market value of the shares exchanged was \$13.58, resulting in a conversion of the Warrants to purchase 48,143 shares of common stock into 8,832 shares of common stock.

## ITEM 6. SELECTED FINANCIAL DATA

The accompanying selected consolidated financial data should be read together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the accompanying consolidated financial statements and related notes that are included in this Annual Report on Form 10-K/A. The following table sets forth selected consolidated financial data as of and for the years in the five-year period ended December 31, 2004: (In thousands, except per share data)

Statement of Operations Data:	2000 <sup>1</sup>	2001	2002	2003	2004
Revenue: Product revenue, net .....	\$ 906	\$ 996	\$ 1,408	\$ 1,805	\$ 291
License and research fees .....	3,235	1,607	7,515	17,635	1,556
Total revenue .....	4,141	2,603	8,923	19,440	1,847
Operating expenses:					
Cost of product revenue .....	358	503	289	498	258
Research and development .....	6,399	6,595	11,613	17,097	21,083
Acquired in-process research and development.....	2,300	—	—	—	—
Royalties .....	1,517	487	9	—	—
Sales and marketing .....	655	595	1,863	2,377	1,046
General and administrative .....	3,247	3,977	8,138	5,679	7,951
Restructuring charge .....	—	—	595	—	—
Total operating expenses .....	14,476	12,157	22,507	25,651	30,338
Loss from operations .....	(10,335)	(9,554)	(13,584)	(6,211)	(28,491)
Gain on sale of product .....	—	—	—	4,236	—
Interest income .....	644	322	278	227	344
Interest expense .....	—	—	(162)	(393)	(462)
Net loss .....	\$ (9,691)	\$ (9,232)	\$ (13,468)	\$ (2,141)	\$ (28,609)
Net loss per common share-basic and diluted.....	\$ (1.51)	\$ (1.16)	\$ (1.34)	\$ (0.20)	\$ (2.21)
Shares used in computing net loss per share.....	6,437	7,956	10,028	10,751	12,955
Balance Sheet Data:	2000	2001	2002	2003	2004 <sup>2</sup>
Cash and short term investments <sup>3</sup> .....	\$ 6,256	\$ 11,760	\$ 9,021	\$ 25,081	\$ 74,474
Working capital .....	5,799	10,404	3,342	14,766	58,362
Total assets .....	11,661	15,440	23,050	31,138	80,775
Notes payable .....	—	—	7,250	6,271	8,352
Accumulated deficit .....	(30,003)	(39,235)	(52,703)	(54,844)	(83,453)
Total stockholders' equity .....	\$ 9,565	\$ 13,494	\$ 8,645	\$ 17,906	\$ 58,148

1. During 2000, Atossa HealthCare was acquired in a transaction that was accounted for under the purchase method. In connection with the acquisition, a charge of \$2.3 million was recognized for acquired in-process research and development.
2. During 2004, we received net proceeds of \$12.3 million from a private placement of 1,136,364 shares of common stock and net proceeds of \$52.9 million from a public offering of 4,250,000 shares of common stock.
3. Includes restricted cash of approximately \$6.3 million at December 31, 2003 and \$9.0 million at December 31, 2004.



## ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

### Overview

*Statements contained herein that are not historical fact may be forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act, that are subject to a variety of risks and uncertainties. There are a number of important factors that could cause actual results to differ materially from those projected or suggested in any forward-looking statement made by us. These factors include, but are not limited to: (i) our ability to obtain additional funding; (ii) our ability to attract and/or maintain manufacturing, research, development and commercialization partners; (iii) our and/or a partner's ability to successfully complete product research and development, including pre-clinical and clinical studies and commercialization; (iv) our and/or a partner's ability to obtain required governmental approvals, including product and patent approvals; and (v) our and/or a partner's ability to develop and commercialize products that can compete favorably with those of competitors. In addition, significant fluctuations in annual or quarterly results may occur as a result of the timing of milestone payments, the recognition of revenue from milestone payments and other sources not related to product sales to third parties, and the timing of costs and expenses related to our research and development programs. Additional factors that would cause actual results to differ materially from those projected or suggested in any forward-looking statements are contained in our filings with the SEC, including those factors discussed under the caption "Risk Factors" in this Report which we urge investors to consider. We undertake no obligation to publicly release revisions in such forward-looking statements that may be made to reflect events or circumstances after the date hereof or to reflect the occurrences of unanticipated events or circumstances, except as otherwise required by securities and other applicable laws.*

We are a pharmaceutical company focusing on development and commercialization of innovative products based on proprietary molecular biology-based intranasal drug delivery technology for delivering both small and large molecule drugs. Using this technology, we create or utilize novel formulation components or excipients that can transiently manipulate or open "tight junctions" between cells in various tissues and thereby allow therapeutic drugs to reach the blood stream. Tight junctions are cell-to-cell connections in various tissues of the body, including epithelial and endothelial layers of the intranasal mucosa, the gastrointestinal tract, and the blood brain barrier. They function to provide barrier integrity and to regulate the transport and passage of molecules across these natural boundaries. This technology is the foundation of our intranasal drug delivery platform, although some of our product candidates utilize our expertise outside this area. Generally, we seek to apply our technology to compounds that we license to, or acquire from, collaborators or other third parties.

We believe our intranasal drug delivery technology offers advantages over injectable routes for the administration of large molecules such as peptides and proteins. These advantages may include improved safety and clinical efficacy and increased patient compliance due to the elimination of injection site pain and avoidance of injection site irritation. In addition, we believe our intranasal drug delivery technology offers advantages over oral administration by providing for faster absorption into the bloodstream, reduced side effects and improved effectiveness by avoiding problems relating to gastrointestinal and liver metabolism. We are utilizing our technologies to develop commercial products, initially with collaboration partners. In select cases, we also plan to internally develop, manufacture and commercialize our products.

We and our collaboration partners are developing a diverse portfolio of product candidates for multiple therapeutic areas including obesity, osteoporosis, breakthrough cancer pain, multiple sclerosis and erectile dysfunction. Our lead product candidate, PYY for obesity, is in Phase I clinical trials and is being developed with our collaboration partner, Merck. Additionally, we are developing two product candidates for the treatment of osteoporosis. PTH<sub>(1-34)</sub> is in Phase I clinical trials, and we have filed an ANDA for our generic calcitonin-salmon intranasal spray which we are developing with our collaboration partner Par Pharmaceutical. As of February 15, 2005, we have 41 patents issued and 161 patent applications filed to protect our proprietary technologies.

As of December 31, 2004, we had an accumulated deficit of \$83.5 million and expect additional operating losses in the foreseeable future as we continue our research and development activities. Our development efforts and the future revenues from sales of these products are expected to generate contract research revenues, milestone payments, license fees, royalties and manufactured product sales for us. As of December 31, 2004, we had approximately \$65.5 million in unrestricted cash, cash equivalents and short term investments. We believe that our current cash position provides us with adequate working capital for approximately 18-24 months, depending upon the degree to which we exploit our various current opportunities that are in the pipeline and the success of our collaborative arrangements. In addition, we are planning to enter into various collaborations to accelerate our R&D programs, and to the extent these collaborations do not occur, we may be required to reduce our research and development activities or raise additional funds from new investors or in the public markets.

In June 2004, we completed the sale of 1,136,364 shares of our common stock, and warrants to purchase up to 511,364 shares of common stock at an exercise price of \$14.40 per share, pursuant to our \$30 million shelf registration statement that was declared effective by the SEC on January 14, 2004. The offering resulted in gross proceeds of approximately \$12.5 million to us prior to the deduction of fees and commissions of \$229,000. The warrants vested on December 25, 2004, and are exercisable until June 25, 2009. At December 31, 2004, the amount remaining available on this shelf registration statement was approximately \$10.1 million.

In December 2004, we completed the public offering of 4,250,000 shares of our common stock at a public offering price of \$13.50 per share pursuant to our \$80 million shelf registration statement that was declared effective by the SEC on October 8, 2004. The offering resulted in gross proceeds of approximately \$57.4 million to us, prior to the deduction of fees and commissions of \$4.5 million. At December 31, 2004, the amount remaining available on this shelf registration statement was approximately \$22.6 million.

### **Critical Accounting Policies and Estimates**

We prepare our consolidated financial statements in conformity with accounting principles generally accepted in the United States of America. As such, we are required to make certain estimates, judgments and assumptions that we believe are reasonable based upon the information available. These estimates and assumptions affect the reported amounts of assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the periods presented. Actual results could differ significantly from those estimates under different assumptions and conditions. We believe that the following discussion addresses our most critical accounting estimates which are those that are most important to the portrayal of our financial condition and results of operations and which require our most difficult and subjective judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. We also have other policies that we consider key accounting policies; however, these policies do not meet the definition of critical accounting estimates, because they do not generally require us to make estimates or judgments which are difficult or subjective.

#### ***Revenue Recognition***

Most of our revenues are generated from research and licensing arrangements. These research and licensing arrangements may include upfront non-refundable payments, development milestone payments, revenue from product manufacturing, payments for research and development services performed and product sales royalties or revenue. Our revenue recognition policies are based on the requirements of SEC Staff Accounting Bulletin No. 104 "Revenue Recognition," and, for contracts with multiple deliverables, we allocate arrangement consideration based on the fair value of the elements under guidance from Emerging Issues Task Force Issue 00-21 ("EITF 00-21"), "Revenue Arrangements with Multiple Deliverables." Under EITF 00-21, revenue arrangements with multiple deliverables are divided into separate units of accounting such as product development and contract manufacturing. Revenue is allocated to these units based upon relative fair values with revenue recognition criteria considered separately for each unit.

Nonrefundable upfront technology license fees, for product candidates where we are providing continuing services related to product development, are deferred and recognized as revenue over the development period or as

we provide the services required under the agreement. The ability to estimate total development effort and costs can vary significantly for each product candidate due to the inherent complexities and uncertainties of drug development. If we cannot estimate the costs to complete development, but can estimate an expected NDA filing date, we will recognize license fee revenue ratably through the NDA filing date. If we are unable to reasonably estimate either total costs to complete development or an expected NDA filing date (performance period), we will defer revenue recognition until one of those estimates can be made or the project is discontinued.

Milestones, in the form of additional license fees, typically represent nonrefundable payments to be received in conjunction with the achievement of a specific event identified in the contract, such as initiation or completion of specified clinical development activities. We believe that a milestone represents the culmination of a distinct earnings process when it is not associated with ongoing research, development or other performance on our part. We recognize such milestones as revenue when they become due and collection is reasonably assured. When a milestone does not represent the culmination of a distinct earnings process, we recognize revenue in manner similar to that of an upfront technology license fee.

The timing and amount of revenue that we recognize from licenses of technology, either from upfront fees or milestones where we are providing continuing services related to product development, is dependent upon our estimates of filing dates or development costs. As product candidates move through the development process, it is necessary to revise these estimates to consider changes to the product development cycle, such as changes in the clinical development plan, regulatory requirements, or various other factors, many of which may be outside of our control. The impact on revenue of changes in our estimates and the timing thereof, is recognized prospectively, over the remaining estimated product development period.

Royalty revenue is generally recognized at the time of product sale by the licensee.

Revenue from research and development services performed is generally received for services performed under collaboration agreements, and is recognized at the time the services are performed. Payments received in excess of amounts earned are recorded as deferred revenue.

Product sales revenue is recognized at the time the manufactured goods are shipped to the purchaser and title has transferred.

#### ***Stock-based compensation***

We apply Accounting Principles Board Opinion No. 25 ("APB 25"), *Accounting for Stock Issued to Employees*, and related interpretations in accounting for our stock-based employee compensation plans, rather than the alternative fair value accounting method provided for under Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation*, ("SFAS 123"). In the Notes to Consolidated Financial Statements, we provide pro-forma disclosures in accordance with SFAS 123 and related pronouncements. Under APB 25, compensation expense is recorded on the date of grant of an option to an employee or member of the Board only if the fair market value of the underlying stock at the time of grant exceeds the exercise price. In the three years ended December 31, 2002, 2003 and 2004, our stock option grants were based on the closing price of our stock on the date of grant, with the exceptions of grants to our chief executive officer in May 2002, and an extension made in October 2002, of the expiration date of certain stock option grants to members of the Board, as described more fully in the Notes to Consolidated Financial Statements. In addition, we have granted options to certain outside consultants, which are required to be measured at fair value and recognized as compensation expense in our Consolidated Statements of Operations. We apply the Black-Scholes option-pricing model for estimating the fair value of options, which involves a number of judgments and variables including estimates of the life of the options and expected volatility which are subject to significant change. A change in the fair value estimate could have a significant effect on the amount of compensation expense calculated.

In June 2004, our 2004 Stock Incentive Plan was approved by our shareholders and, subsequently, restricted stock grants have been issued to certain directors and employees. Non-cash compensation expense is being recognized over the applicable vesting periods of one to three years of the restricted shares.

In December 2004, the Financial Accounting Standards Board ("FASB") released its final revised standard, SFAS No. 123R (SFAS 123R), *Share-Based Payment*. SFAS 123R requires that a public entity measure the cost of equity based service awards based on the grant-date fair value of the award. That cost will be recognized over the period during which an employee is required to provide service in exchange for the award or the vesting period. A public entity will initially measure the cost of liability based service awards based on its current fair value and the fair value of that award will be remeasured subsequently at each reporting date through the settlement date. Changes in fair value during the requisite service period will be recognized as compensation cost over that period. Adoption of SFAS 123R is required for fiscal periods beginning after June 15, 2005. We are evaluating SFAS 123R and believe it will likely result in recognition of additional non-cash stock-based compensation expense and accordingly would increase net loss in amounts which likely will be considered material. There will be no effect on cash, working capital or total stockholders' equity.

### ***Income Taxes***

A critical estimate is the full valuation allowance for deferred taxes that was recorded based on the uncertainty that such tax benefits will be realized in future periods. To the extent we achieve profitability such deferred tax allowance would be reversed at that time.

### ***Clinical Trial Expenses***

Clinical trial expenses, which are included in research and development expenses, represent obligations resulting from our contracts with various clinical research organizations in connection with conducting clinical trials for our product candidates. We recognize expenses for these contracted activities based on a variety of factors, including actual and estimated labor hours, clinical site initiation activities, patient enrollment rates, estimates of external costs and other activity-based factors. We believe that this method best approximates the efforts expended on a clinical trial with the expenses we record. We adjust our rate of clinical expense recognition if actual results differ from our estimates.

### **Results of Operations**

#### ***Total Revenue***

The following table sets forth revenue information:

	Years Ended December 31,					
	2002		2003		2004	
			(in thousands)			
	Revenue	% of Total	Revenue	% of Total	Revenue	% of Total
Product revenue, net .....	\$ 1,408	16%	\$ 1,805	9%	\$ 291	16%
License and research fees .....	<u>7,515</u>	<u>84%</u>	<u>17,635</u>	<u>91%</u>	<u>1,556</u>	<u>84%</u>
Total .....	<u>\$ 8,923</u>	<u>100%</u>	<u>\$ 19,440</u>	<u>100%</u>	<u>\$ 1,847</u>	<u>100%</u>
Percentage increase (decrease) .....			118%		(90%)	

Our total revenue was significantly lower in 2004 compared to 2003, primarily because of license and research fees received by us and recognition of previously deferred amounts in 2003 as a result of the divestiture agreement with Pharmacia in January 2003, pursuant to which we reacquired all rights to the intranasal apomorphine product. The 118% increase in total revenue in 2003 compared to 2002 was driven primarily by an increase in license and research fees as a result of the divestiture agreement with Pharmacia, and to a lesser extent from fees from services

performed for Questcor in filing the New Drug Application ("NDA") for the Nascobal® spray product totaling approximately \$1.0 million.

### ***License and Research Fees***

The following table sets forth license and research fees:

	<b>Years Ended December 31,</b>		
	<b>2002</b>	<b>2003</b>	<b>2004</b>
	<b>(in thousands)</b>		
License fees and research and development services fees recognized under the collaboration and license agreement with Merck .....	—	—	\$ 1,257
Revenue received under the divestiture agreement with Pharmacia:			
Divestiture payment.....	—	\$ 6,000	—
Research funds received at time of divestiture.....	—	7,000	—
Revenue received under the collaboration and license agreement with Pharmacia:			
License fee revenue recognized.....	\$ 1,749	3,251	—
Milestone payments.....	3,000	—	—
Research and development services performed.....	<u>2,620</u>	<u>11</u>	<u>—</u>
Subtotal of Pharmacia-related revenue .....	7,369	16,262	—
Other license and research fees.....	<u>146</u>	<u>1,373</u>	<u>299</u>
Total license and research fees .....	<u>\$ 7,515</u>	<u>\$ 17,635</u>	<u>\$ 1,556</u>

Our license and research fee revenue recognized in 2004 is primarily composed of amortization over the estimated development periods of the \$5.0 million license fee received from Merck in October 2004 and of the license fee received from Par Pharmaceutical in October 2004, and fees recognized from other collaboration and license agreements. The estimated development periods may be revised over time based upon changes in clinical development plans, regulatory requirements or other factors, many of which may be out of our control.

A significant portion of our license and research fees in 2003 and 2002 came from revenue received under the collaboration and license agreement and the divestiture agreement with Pharmacia, representing 84% of total revenue in 2003 and 83% of total revenue in 2002. We entered into a collaboration and license agreement with Pharmacia in February 2002, pursuant to which Pharmacia received exclusive worldwide rights to develop and market intranasal apomorphine product for the treatment of male and female sexual dysfunction. Under the agreement, we received \$5.0 million in 2002 which we amortized over the estimated development period. Upon termination of the collaboration and license agreement in April 2003, we recognized all remaining deferred revenues. Accordingly, we recognized \$1.8 million in 2002 and \$3.3 million in 2003 as license and research fees.

We also recognized an aggregate of \$3.0 million in 2002 as license and research fees for achieving development milestones under the collaboration and license agreement. In addition, Pharmacia agreed to pay us for certain research and development costs for activities conducted by us since the execution of the collaboration and license agreement, and we recognized \$2.6 million in 2002 and \$11,000 in 2003 as license and research fees related to such activities.

We entered into a divestiture agreement with Pharmacia in January 2003, under which we reacquired all rights to the intranasal apomorphine products that were previously granted to Pharmacia under a collaboration and license agreement in February 2002. Under the divestiture agreement, Pharmacia made a cash payment of \$13.5 million consisting of a \$6.0 million divestiture payment, \$7.0 million research and development funds and \$0.5 million for reimbursement of expenses of the divestiture transaction. We recognized \$13.0 million of such payments as license and research fees in 2003. We did not recognize any revenue from Pharmacia during 2004.

### Product Revenue and Cost of Product Revenue

The following table sets forth information on product revenue, cost of product revenue and cost of product revenue as a percentage of product revenue:

	Years Ended December 31,		
	2002	2003	2004
	(in thousands)		
Product revenue .....	\$ 1,408	\$ 1,805	\$ 291
Cost of product revenue .....	289	498	258
Cost of product revenue as a percentage of product revenue .....	21%	28%	89%

Product revenue consists of sales of Nascobal® nasal gel and royalty revenue from sales of Nascobal® nasal gel. From 1997 until September 30, 2002, we granted to Schwarz Pharma, Inc. ("Schwarz Pharma") exclusive rights to market Nascobal® in the U.S. while retaining worldwide manufacturing rights. Accordingly, we recorded revenue from sales of manufactured Nascobal® nasal gel to Schwarz Pharma and royalty revenue received from Schwarz Pharma. On September 30, 2002, we terminated the license agreement with Schwarz Pharma and reacquired rights to Nascobal® nasal gel. During the period from October 1, 2002 to June 17, 2003, we earned revenue from our own direct sales of Nascobal® nasal gel to drug wholesalers using a contract sales organization and a contract distributor. On June 17, 2003, we completed the sale of the assets relating to our Nascobal® brand products, including the Nascobal® nasal gel, to Questcor. In connection with the sale, we entered into a supply agreement with Questcor under which Questcor is obligated to purchase from us all of its requirements for the Nascobal® nasal gel and, upon FDA approval, the Nascobal® nasal spray. Since the sale, we earn product sales revenue under the supply agreement and we expect to receive product sales revenue under this supply agreement in the future.

Primarily as a result of the change described above, product revenue decreased by 84% in 2004 compared to 2003, and gross margin decreased to 11% in 2004 compared to 72% in 2003. The 72% increase in cost of product revenue in 2003 compared to 2002 was driven, in part, by an increase in product revenue as a result of our own direct sales of Nascobal® nasal gel from October 1, 2002 to June 17, 2003. The cost of product revenue as a percentage of product revenue increased to 28% in 2003 from 21% in 2002, primarily due to the inclusion of \$0.3 million of royalty revenue in 2002 in product revenue on which no cost of product revenue was recorded.

### Research and Development

Research and development expense consists primarily of salaries and other personnel-related expenses, costs of clinical trials, consulting and other outside service, laboratory supplies, facilities costs, FDA filing fees and other costs. Research and development expense by project as a percentage of total research and development project expense, and total research and development expense, are as follows:

	Years Ended December 31,		
	2002	2003	2004
	(in thousands)		
PYY .....	1%	14%	42%
Calcitonin .....	6%	32%	18%
Tight Junctions and RNAi .....	—	8%	22%
PTH <sub>(1-34)</sub> .....	—	—	7%
Apomorphine .....	47%	25%	3%
Other research and development projects(1) .....	46%	21%	8%
	<u>100%</u>	<u>100%</u>	<u>100%</u>
Total R&D expense .....	\$ 11,613	\$ 17,097	\$ 21,083
Dollar increase .....		5,484	3,986
Percentage increase .....		47%	23%

- 
- (1) Other research and development projects include our oral abuse-resistant opioid, Morphine Gluconate and other projects.

The 23% increase in research and development expense in 2004 compared to 2003 resulted primarily from the following:

- Personnel-related expenses increased by 33% to \$8.9 million compared to \$6.7 million in 2003 due to an increase in personnel supporting our research and development programs.
- Costs of clinical trials, consulting, outside services and laboratory supplies increased by 4% to \$7.4 million in 2004 compared to \$7.1 million in 2003 due primarily to the timing of clinical trials performed for our PYY, calcitonin, RNAi, PTH and intranasal apomorphine products under development.
- Research and development administrative expenses increased by 116% to \$1.3 million in 2004 compared to \$0.6 million in 2003 due primarily to an increase in licensing of third-party patent technologies including patent licenses from Thiakis, Cedars-Sinai and the University of Cincinnati.
- Facilities and equipment costs increased by 26% to \$3.4 million in 2004 compared to \$2.7 million in 2003 due to rent and related expenses on additional space leased at the Bothell facility and an increase in depreciation of equipment resulting from additional capital expenditures.

The 47% increase in research and development expense in 2003 compared to 2002 resulted primarily from the following:

- Personnel-related expenses increased by 52% to \$6.7 million in 2003 compared to \$4.4 million in 2002 due to an increase in research and development activities for our products under development and our tight junctions technology.
- Costs of clinical trials, consulting, outside services and laboratory supplies increased by 39% to \$7.1 million in 2003 compared to \$5.1 million in 2002 due to clinical trials performed for our intranasal apomorphine and PYY products under development.
- Facilities costs increased by 50% to \$2.7 million in 2003 compared to \$1.8 million in 2002 due to rent and related expenses of the Bothell facility, offset in part by closure of the Adams Avenue facility in the fourth fiscal quarter of 2002.
- FDA filing fees in 2003 were approximately \$0.3 million due to the filing of the NDA for the Nascobal® nasal spray. There were no FDA filing fees in 2002.

We expect a continued increase in research and development expense in the foreseeable future as we continue to expand our research and development activities. These expenditures are subject to uncertainties in timing and cost to completion. We test compounds in numerous preclinical studies for safety, toxicology and efficacy. We then conduct early stage clinical trials for each drug candidate. If we are not able to engage a collaboration partner prior to the commencement of later stage clinical trials, or if we decide to pursue a strategy of maintaining commercialization rights to a program, we may fund these trials ourselves. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain products in order to focus our resources on more promising products. Completion of clinical trials by us and our collaboration partners may take several years or more, but the length of time varies substantially according to the type, complexity, novelty and intended use of a drug candidate. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including:

- the number of sites included in the clinical trials;

- the length of time required to enroll suitable patient subjects;
- the number of patients that participate in the trials;
- the duration of patient follow-up that seems appropriate in view of results; and
- the number and complexity of safety and efficacy parameters monitored during the study.

None of our current product candidates has received FDA or foreign regulatory marketing approval. In order to achieve marketing approval, the FDA or foreign regulatory agencies must conclude that our and our collaboration partners' clinical data establishes the safety and efficacy of our drug candidates. Furthermore, our strategy includes entering into collaborations with third parties to participate in the development and commercialization of our products. In the event that the collaboration partner has control over the development process for a product, the estimated completion date would largely be under control of such partner. We cannot forecast with any degree of certainty how such collaboration arrangements will affect our development plans or capital requirements.

As a result of the uncertainties discussed above, we are often unable to determine the duration and completion costs of our research and development projects or when and to what extent we will receive cash inflows from the commercialization and sale of a product.

### ***Sales and Marketing***

Sales and marketing expense consists primarily of salaries and other personnel-related expenses, costs of using a contract sales organization and a contract distributor for Nascobal® nasal gel, consulting, sales materials, trade shows and advertising. Total sales and marketing expense and dollar and percentage changes are as follows:

	<b>Years Ended December 31,</b>		
	<b>2002</b>	<b>2003</b>	<b>2004</b>
	<b>(in thousands)</b>		
Total sales and marketing expense .....	\$ 1,863	\$ 2,377	\$ 1,046
Dollar increase (decrease).....		514	(1,331)
Percentage increase (decrease) .....		28%	(56%)

The 56% decrease in sales and marketing expenses in 2004 compared to 2003 resulted primarily from reduced sales and marketing expenses following the sale of the assets relating to our Nascobal® brand products to Questcor in June 2003. In the first six months of 2003, we incurred costs associated with marketing programs to support our own direct sales of Nascobal® nasal gel prior to our sale of the assets relating to our Nascobal® brand. We expect sales and marketing costs, which includes business development staff and activities, to increase moderately in the foreseeable future to support activities associated with partnering our other drug candidates.

In October 2002, after we terminated the agreement with Schwarz Pharma and reacquired rights to Nascobal® nasal gel, we initiated marketing programs to re-launch direct sales of Nascobal® nasal gel. The 28% increase in sales and marketing expense in 2003 compared to 2002 was primarily due to expenses incurred as part of this re-launch. In June 2003, we discontinued direct sales of Nascobal® nasal gel.



## General and Administrative

General and administrative expense consists primarily of salaries and other personnel-related expenses to support our research and development activities, amortization of non-cash deferred stock option and restricted stock compensation, professional fees such as accounting and legal, corporate insurance, amortization of intangibles and facilities costs. Total general and administrative expense and dollar and percentage changes are as follows:

	Years Ended December 31,		
	2002	2003	2004
		(in thousands)	
Total general and administrative expense.....	\$ 8,138	\$ 5,679	\$ 7,951
Dollar increase (decrease).....		(2,459)	2,272
Percentage increase (decrease) .....		(30%)	40%

The 40% increase in general and administrative expenses in 2004 compared to 2003 resulted primarily from the following:

- Costs of legal fees, accounting fees, corporate insurance and other administrative costs increased by 48% to \$3.7 million in 2004 compared to \$2.5 million in 2003. This was due primarily to increases in legal and accounting fees, corporate insurance, non-cash stock compensation expense related to restricted stock grants and other administrative costs. In addition, 2003 included a \$0.5 million expense reduction related to the reimbursement of legal expenses received as part of the divestiture agreement with Pharmacia.
- Amortization of non-cash deferred stock compensation increased by 80% to approximately \$0.9 million in 2004 compared to \$0.4 million in 2003, primarily due to the expensing of restricted stock which was first issued in 2004.
- Personnel-related expenses increased by 25% to \$3.0 million in 2004 compared to \$2.4 million in 2003 due primarily to increased headcount related to administrative activities.

The 30% decrease in general and administrative expenses in 2003 compared to 2002 resulted primarily from the following:

- Costs of legal fees, accounting fees, corporate insurance and other administrative costs decreased by 43% to \$2.1 million in 2003 compared to \$3.7 million in 2002. In January 2003, we entered into a divestiture agreement with Pharmacia under which we reacquired all rights to the intranasal apomorphine product. In preparation of this transaction, we incurred significant legal costs in 2002. In 2003, as part of the divestiture agreement, we received and recorded a \$0.5 million legal cost reimbursement from Pharmacia. Patent legal fees decreased by \$0.4 million in 2003 compared to 2002 due to the addition of an in-house patent counsel in 2003.
- Amortization of non-cash deferred stock option compensation decreased by 64% to approximately \$0.5 million in 2003 compared to \$1.4 million in 2002. We recorded approximately \$0.5 million of non-cash compensation expense in 2003 and \$0.8 million in 2002 related to stock options granted to our Chief Executive Officer in connection with the extension of his employment agreement through December 31, 2005, as well as approximately \$0.6 million of compensation expense in 2002 related to extending the expiration dates for all options held by certain members of the Board.
- Facilities costs decreased by 33% to \$0.4 million in 2003 compared to \$0.6 million in 2002 primarily due to the closure of our prior headquarters facility on Long Island, NY in the fourth quarter of 2002.
- Personnel-related expenses increased by 4% to \$2.4 million in 2003 compared to \$2.3 million in 2002 primarily due to increased headcount.

- Amortization of intangibles increased by 100% to \$0.4 million in 2003 compared to \$0.2 million in 2002 due to amortization of the Nascobal® related assets. In June 2003, we completed the sale of the assets relating to our Nascobal® brand products to Questcor, at which time the amortization ceased.

We expect general and administrative expenses to remain stable or to increase in the foreseeable future, depending on the growth of our research and development and other corporate activities.

### ***Restructuring Charge***

In 2002, we recorded a restructuring charge of approximately \$0.6 million relating to the termination of the lease of our prior headquarters facility on Long Island, NY. The restructuring charge was comprised of approximately \$0.9 million in a write-off of leasehold improvements and approximately \$0.1 million for additional costs related to vacating the facility, which was partially offset by an elimination of approximately \$0.4 million in deferred rent liability. We did not incur restructuring charges in 2003 or 2004.

### ***Gain on Sale of Product***

In 2003, we recognized a gain of approximately \$4.2 million on the sale of the assets related to our Nascobal® brand products to Questcor. The gain was calculated as \$14.0 million in non-contingent proceeds, less the net book value of assets of \$8.1 million, less costs and fees. At the time of the sale, approximately \$1.0 million of gain relating to the fair value of work to be completed on the NDA filing for the Nascobal® nasal spray product was deferred and later recognized in 2003 as license and research fee revenue.

### ***Interest Income***

The following table sets forth information on interest income, average funds available for investment and average interest rate earned:

	<b>Years Ended December 31,</b>		
	<b>2002</b>	<b>2003</b>	<b>2004</b>
	<b>(in thousands)</b>		
Interest income .....	\$ 278	\$ 227	\$ 344
Average funds available for investment .....	14,200	18,200	24,100
Average interest rate .....	2.0%	1.2%	1.4%

The 52% increase in interest income in 2004 compared to 2003 was primarily due to higher average balances available for investment. The 18% decrease in interest income in 2003 compared to 2002 was due primarily to a decrease in the average interest rate earned on funds available for investment due to a decrease in the prevailing market interest rates.

### ***Interest Expense***

We incur interest expense on our capital leases and notes payable. The following table sets forth information on interest expense, average borrowings and average interest rate earned:

	<b>Year Ended December 31,</b>		
	<b>2002</b>	<b>2003</b>	<b>2004</b>
	<b>(in thousands)</b>		
Interest expense .....	\$ 162	\$ 393	\$ 414
Average borrowings under capital leases and notes payable .....	2,400	8,000	10,600
Average interest rate .....	6.8%	4.9%	3.9%

The 5% increase in interest expense in 2004 compared to 2003 was due to an increase in the average borrowings partially offset by lower average interest rates. In 2004, average borrowings under the Wells Fargo note were approximately \$7.8 million, at rates averaging approximately 2.3%, and average borrowings under the GE Capital

leases were approximately \$2.8 million, at rates ranging from approximately 8.3% to 10.0%. In 2003, average borrowings under the Schwarz Pharma and Wells Fargo notes were approximately \$7.0 million, at interest rates ranging from 1.5% to 7.5%, and average borrowings under the GE Capital leases were approximately \$1.0 million, at interest rates ranging from approximately 8.3% to 10.0%.

The 143% increase in interest expense in 2003 compared to 2002 was driven primarily by a 233% increase in the average borrowings, partially offset by a decrease in the average interest rate. In June 2003, we paid off the note payable to Schwarz Pharma, which had an interest rate of 7.5%, in connection with our sale of the assets relating to our Nascobal® brand products to Questcor. In June 2003, we entered into a note payable with Wells Fargo Bank with an initial balance of \$7.0 million at a rate of LIBOR plus 0.75%. The rate paid on the Wells Fargo note ranged from 1.9% to 2.0% in 2003. We also increased borrowings on our capital leases in 2003 by approximately \$2.4 million at interest rates ranging from 8.3% to 8.6%.

## **Liquidity and Capital Resources**

### ***Cash Requirements***

Our capital requirements consist primarily of the need for working capital, including funding research and development activities and capital expenditures for the purchase of equipment. From time to time, we may also require capital for investments involving acquisitions and strategic relationships. We have an accumulated deficit of approximately \$83.5 million as of December 31, 2004 and expect additional operating losses in the foreseeable future as we continue to expand our research and development activities. In addition, we are planning to enter into various collaborations in furtherance of our research and development programs, and we may be required to reduce our research and development activities or raise additional funds from new investors or in the public markets.

We also have contractual obligations in the form of facility leases, notes payable and capital leases. See "Liquidity and Capital Resources — Contractual Obligations."

### ***Sources and Uses of Cash***

We have financed our operations primarily through the sale of common stock and warrants through private placements and in the public markets, revenues received from our collaboration partners, equipment financing facilities and notes payable.

On December 18, 2003, we filed a shelf registration statement with the SEC, which was declared effective by the SEC on January 14, 2004, pursuant to which we may issue common stock or warrants, up to an aggregate of \$30 million. On September 30, 2004 we filed another shelf registration statement with the SEC, which was declared effective by the SEC on October 8, 2004, pursuant to which we may issue common stock, warrants or debt securities, up to an aggregate of \$80 million. These shelf registration statements enable us to raise capital from the offering of securities covered by the shelf registration statements, as well as any combination thereof, from time to time and through one or more methods of distribution, subject to market conditions and our cash needs.

In June 2004, we completed the sale of 1,136,364 shares of our common stock, and warrants to purchase up to 511,364 shares of common stock at an exercise price of \$14.40 per share, pursuant to our \$30 million effective shelf registration statement. The offering resulted in gross proceeds of approximately \$12.5 million to us prior to the deduction of fees and commissions of \$229,000. The warrants vested on December 25, 2004, and are exercisable until June 25, 2009. At December 31, 2004, the amount remaining available on this shelf registration statement was approximately \$10.1 million.

In December 2004, we completed the public offering of 4,250,000 shares of our common stock at a public offering price of \$13.50 per share pursuant to our \$80 million effective shelf registration statement. The offering resulted in gross proceeds of approximately \$57.4 million to us, prior to the deduction of fees and commissions of

\$4.5 million. At December 31, 2004, the amount remaining available on this shelf registration statement was approximately \$22.6 million.

Our research and development efforts and collaborative arrangements with our partners enable us to generate contract research revenues, milestone payments, license fees, royalties and manufactured product sales for us.

- Under our collaborative arrangement with Merck, we received an initial cash payment of \$5 million in October 2004. The \$5 million initial payment is being amortized over the estimated development period. We are also eligible to receive milestone payments upon achievement of specified product development goals or sales targets. If certain development and approval milestones are achieved, we will be eligible to receive up to \$131 million from Merck. If certain sales related milestones are achieved, we will be eligible to receive up to an additional \$210 million from Merck, subject to certain other conditions. Merck will also pay us for manufacturing-related development activities and will purchase from us clinical supply and finished product. We will also receive royalties on product sales based on certain sales-related thresholds.
- Under our collaborative arrangement with Par Pharmaceutical, we received an initial cash payment which is being amortized over the estimated development period. We expect in the future to receive additional revenue from Par Pharmaceutical in the form of milestone payments, product transfer payments for manufactured product and a profit sharing upon commercialization of generic calcitonin-salmon intranasal spray.

Total sources and uses of cash are as follows:

	Years Ended December 31,		
	2002	2003	2004
	(in thousands)		
Cash used in operating activities .....	\$ (6,504)	\$ (7,686)	\$ (19,168)
Cash provided by (used in) investing activities .....	(3,820)	3,482	(33,553)
Cash provided by financing activities .....	7,585	5,704	67,997
Net increase (decrease) in cash and cash equivalents .....	\$ (2,739)	\$ 1,500	\$ 15,276

We used cash of \$19.2 million in our operating activities in 2004, compared to \$7.7 million in 2003 and \$6.5 million in 2002. Cash used in operating activities relates primarily to funding net losses and changes in deferred revenue from collaborators, accounts and other receivables, and accrued expenses and other liabilities, partially offset by depreciation and amortization and non-cash compensation related to restricted stock and stock options. We also recognized a gain on sale of product of \$4.2 million in 2003 from our sale of the assets relating to our Nascobal® brand products to Questcor. We expect to use cash for operating activities in the foreseeable future as we continue our research and development activities.

Our investing activities used cash of \$33.6 million in 2004, compared to providing cash of \$3.5 million in 2003 and to using cash of \$3.8 million in 2002. Changes in cash from investing activities are due primarily to purchases of short-term investments net of maturities and purchases of property and equipment. In addition, our sale of the assets relating to our Nascobal® brand products to Questcor resulted in a cash inflow of \$14.0 million in 2003. We expect to continue to make significant investments in our research and development infrastructure, including purchases of property and equipment to support our research and development activities.

Our financing activities provided cash of \$68.0 million in 2004, compared to \$5.7 million in 2003 and \$7.6 million in 2002. Changes in cash from financing activities are primarily due to issuance of common stock and warrants, issuance of notes payable, proceeds from equipment financing facilities and exercises of stock options and warrants. We raised net proceeds of approximately \$65.2 million in 2004, \$10.0 million in 2003 and \$5.0 million in 2002 through public and private placements of common shares and warrants.

### ***Liquidity***

We had a working capital (current assets minus current liabilities) surplus of \$58.4 million as of December 31, 2004 and \$14.8 million as of December 31, 2003. As of December 31, 2004, we had approximately \$74.5 million in cash, cash-equivalents and short-term investments, including \$9.0 million in restricted cash. We believe, although there can be no assurance, that our current cash position provides us with adequate working capital for the next 18 to 24 months, depending upon the degree to which we exploit our various current opportunities that are in the pipeline and the success of our collaborative arrangements. This belief is based, in part, on the assumption that we have completed and are planning to enter into various collaborations to accelerate our research and development programs which will provide us with additional financing. To the extent these collaborations do not proceed as planned, we may be required to reduce our research and development activities or, if necessary and possible, raise additional capital from new investors or in the public markets.

As of February 22, 2005, we had unused credit lines of approximately \$14.5 million out of total available credit lines of approximately \$15.5 million. Our credit line with Wells Fargo expires December 31, 2005. Our loan balance of approximately \$8.4 million was paid in full on February 18, 2005. Our available lease line with GE Capital of \$4.0 million expires December 31, 2005.

### ***Contractual Obligations***

We have contractual obligations in the form of facility leases, notes payable, capital leases and purchase obligations. The following chart summarizes the principal payment component of our contractual obligations at December 31, 2004:

(in thousands)	<u>Total</u>	<u>2005</u>	<u>2006</u>	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>Thereafter</u>
Facility leases .....	\$ 20,373	\$ 1,661	\$ 1,655	\$ 1,696	\$ 1,738	\$ 1,782	\$ 11,841
Note payable .....	8,352	8,352	—	—	—	—	—
Capital lease obligations .....	3,251	1,532	1,286	433	—	—	—
Purchase obligations .....	214	214	—	—	—	—	—
Total .....	<u>\$ 32,190</u>	<u>\$ 11,759</u>	<u>\$ 2,941</u>	<u>\$ 2,129</u>	<u>\$ 1,738</u>	<u>\$ 1,782</u>	<u>\$ 11,841</u>

The following chart summarizes interest on our contractual obligations at December 31, 2004:

(in thousands)	<u>Total</u>	<u>2005</u>	<u>2006</u>	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>Thereafter</u>
Note payable .....	\$ 271	\$ 271	—	—	—	—	—
Capital lease obligations .....	331	221	\$ 94	\$ 16	—	—	—
Total .....	<u>\$ 602</u>	<u>\$ 492</u>	<u>\$ 94</u>	<u>\$ 16</u>	<u>—</u>	<u>—</u>	<u>—</u>

### ***Off-Balance Sheet Arrangements***

As of December 31, 2004, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of SEC Regulation S-K.

### ***Recent Accounting Pronouncements***

In November 2004, the FASB issued SFAS 151 ("SFAS 151"), "Inventory Costs, an amendment of ARB No. 43, Chapter 4". The standard requires that abnormal amounts of idle capacity and spoilage costs should be excluded from the cost of inventory and expensed when incurred. The provision is effective for fiscal periods beginning after June 15, 2005. We do not expect the adoption of this standard to have a material effect on our consolidated financial statements.

In December 2004, the FASB issued SFAS 153 ("SFAS 153"), "Exchanges of Nonmonetary Assets, an amendment of APB No. 29, Accounting for Nonmonetary Transactions." SFAS 153 requires exchanges of productive assets to be accounted for at fair value, rather than at carryover basis, unless (1) neither the asset received

nor the asset surrendered has a fair value that is determinable within reasonable limits or (2) the transactions lack commercial substance. SFAS 153 is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. We do not expect the adoption of this standard to have a material effect on our consolidated financial statements.

In December 2004, the FASB released its final revised standard, SFAS No. 123R (SFAS 123R"), "*Share-Based Payment*." SFAS 123R requires that a public entity measure the cost of equity based service awards based on the grant-date fair value of the award. That cost will be recognized over the period during which an employee is required to provide service in exchange for the award or the vesting period. A public entity will initially measure the cost of liability based service awards based on its current fair value and the fair value of that award will be remeasured subsequently at each reporting date through the settlement date. Changes in fair value during the requisite service period will be recognized as compensation cost over that period. Adoption of SFAS 123R is required for fiscal periods beginning after June 15, 2005. We are evaluating SFAS 123R and believe it will likely result in recognition of additional non-cash stock-based compensation expense and, accordingly, would increase net loss in amounts which likely will be considered material.

#### ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our exposure to market rate risk for changes in interest rates relates primarily to our investment of cash in excess of near term requirements. We have a prescribed methodology whereby we invest our excess cash in debt instruments of U.S. government agencies and high quality corporate issuers (Standard & Poor's double "AA" rating and higher). To mitigate market risk, securities have a maturity date within 18 months, no category of issue can exceed 50% of the portfolio, and holdings of any one issuer excluding the U.S. government do not exceed 20% of the portfolio. Periodically, the portfolio is reviewed and adjusted if the credit rating of a security held has deteriorated. We do not utilize derivative financial instruments.

Our revolving line of credit note with Wells Fargo Bank requires monthly payments of interest, which is payable at 1.5% below prime, if not fixed for one, two or three months at 0.75% above LIBOR. At December 31, 2004, the interest rate was fixed for a 90-day term at 3.25%. On February 18, 2005, the note payable was paid in full. The entire note balance, if any, is due and payable December 31, 2005. Capital lease obligations bear interest at fixed rates ranging from 8.3% to 10.0%. The table below outlines the minimum cash outflows for payments on the note payable and capital lease obligations (in thousands) as described in further detail in the Notes to Consolidated Financial Statements.

	<u>2005</u>	<u>2006</u>	<u>2007</u>	<u>Thereafter</u>	<u>Total</u>	<u>Fair Value</u>
Note payable - principal .....	\$ 8,352	—	—	—	\$ 8,352	\$ 8,352
Note payable - interest.....	271				271	271
Capital lease obligations - principal.....	1,532	\$ 1,286	\$ 433	—	3,251	3,239
Capital lease obligations - interest.....	221	94	16		331	356
Total.....	<u>\$ 10,376</u>	<u>\$ 1,380</u>	<u>\$ 449</u>	<u>—</u>	<u>\$ 12,205</u>	<u>\$ 12,218</u>

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

<b>REPORTS OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM .....</b>	<b>50-52</b>
<b>FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA</b>	
Consolidated Balance Sheets at December 31, 2003 and 2004 .....	53
Consolidated Statements of Operations for the years ended December 31, 2002, 2003 and 2004 .....	54
Consolidated Statements of Stockholders' Equity for the years ended December 31, 2002, 2003 and 2004 .	55
Consolidated Statements of Cash Flows for the years ended December 31, 2002, 2003 and 2004 .....	56
Notes to Consolidated Financial Statements .....	57-73

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders  
Nastech Pharmaceutical Company Inc.:

We have audited the accompanying consolidated balance sheets of Nastech Pharmaceutical Company Inc. (the "Company") and subsidiary as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity and comprehensive loss, and cash flows for each of the years in the three-year period ended December 31, 2004. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Nastech Pharmaceutical Company Inc. and subsidiary as of December 31, 2004 and 2003, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Nastech Pharmaceutical Company Inc. and subsidiary's internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated February 18, 2005 expressed an unqualified opinion on management's assessment of, and the effective operation of, internal control over financial reporting.

/s/ KPMG LLP

Seattle, WA  
February 18, 2005



## **Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders  
Nastech Pharmaceutical Company Inc.:

We have audited management's assessment, included in the accompanying Management Report on Internal Control, that Nastech Pharmaceutical Company Inc. and subsidiary (the "Company") maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that the Company maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commissions (COSO). Also, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Natesth Pharmaceutical Company Inc. and subsidiary as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity and comprehensive loss, and cash flows for each of the years in the three-year period ended December 31, 2004, and our report dated February 18, 2005 expressed an unqualified opinion on those consolidated financial statements.

/s/ KPMG LLP

Seattle, WA  
February 18, 2005

**NASTECH PHARMACEUTICAL COMPANY INC. AND SUBSIDIARY**  
**CONSOLIDATED BALANCE SHEETS**  
(In Thousands, Except Share and Per Share Data)

	December 31, 2003	December 31, 2004
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents .....	\$ 10,521	\$ 25,797
Restricted cash .....	6,271	9,000
Short term investments .....	8,289	39,677
Accounts receivable, net .....	89	—
Inventories .....	180	57
Prepaid expenses and other current assets .....	484	674
Total current assets .....	25,834	75,205
Property and equipment, net .....	4,474	5,160
Security deposits and other assets .....	830	410
Total assets .....	<u>\$ 31,138</u>	<u>\$ 80,775</u>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable .....	\$ 2,390	\$ 1,652
Accrued expenses and other liabilities .....	1,510	2,533
Notes payable .....	6,271	8,352
Capital lease obligations - current portion .....	897	1,532
Deferred revenue - current portion .....	—	2,774
Total current liabilities .....	11,068	16,843
Capital lease obligations, net of current portion .....	1,569	1,719
Deferred revenue, net of current portion .....	—	3,483
Other liabilities .....	595	582
Total liabilities .....	<u>13,232</u>	<u>22,627</u>
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$.01 par value; 100,000 authorized: no shares issued and outstanding .....	—	—
Common stock, \$.006 par value; 25,000,000 authorized: 11,849,128 and 17,895,976 shares outstanding at December 31, 2003 and 2004, respectively .....	71	107
Additional paid-in capital .....	73,428	142,853
Deferred compensation .....	(749)	(1,358)
Accumulated deficit .....	(54,844)	(83,453)
Accumulated other comprehensive loss .....	—	(1)
Total stockholders' equity .....	17,906	58,148
Total liabilities and stockholders' equity .....	<u>\$ 31,138</u>	<u>\$ 80,775</u>

See accompanying notes to consolidated financial statements.

**NASTECH PHARMACEUTICAL COMPANY INC. AND SUBSIDIARY**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**  
(In Thousands, Except Per Share Data)

	<u>Years Ended December 31,</u>		
	<u>2002</u>	<u>2003</u>	<u>2004</u>
Revenue:			
Product revenue, net .....	\$ 1,408	\$ 1,805	\$ 291
License and research fees .....	<u>7,515</u>	<u>17,635</u>	<u>1,556</u>
Total revenue .....	8,923	19,440	1,847
Operating expense:			
Cost of product revenue .....	289	498	258
Research and development .....	11,613	17,097	21,083
Sales and marketing .....	1,863	2,377	1,046
General and administrative .....	8,138	5,679	7,951
Royalties .....	9	—	—
Restructuring charge .....	<u>595</u>	<u>—</u>	<u>—</u>
Total operating expenses .....	<u>22,507</u>	<u>25,651</u>	<u>30,338</u>
Loss from operations .....	(13,584)	(6,211)	(28,491)
Gain on sale of product .....	—	4,236	—
Interest income .....	278	227	344
Interest and other expense .....	(162)	(393)	(462)
Net loss .....	<u>\$ (13,468)</u>	<u>\$ (2,141)</u>	<u>\$ (28,609)</u>
Net loss per common share - basic and diluted .....	<u>\$ (1.34)</u>	<u>\$ (0.20)</u>	<u>\$ (2.21)</u>
Shares used in computing net loss per share - basic and diluted .....	<u>10,028</u>	<u>10,751</u>	<u>12,955</u>

See accompanying notes to consolidated financial statements.

**NASTECH PHARMACEUTICAL COMPANY INC. AND SUBSIDIARY**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY AND COMPREHENSIVE LOSS**  
For the Years Ended December 31, 2002, 2003 and 2004  
(In Thousands, Except Share Data)

	<u>Common Stock</u>		<u>Additional Paid-in Capital</u>	<u>Deferred Compensation</u>	<u>Accumulated Deficit</u>	<u>Accumulated Other Comprehensive Loss</u>	<u>Treasury Stock</u>	<u>Total Stockholders' Equity</u>
	<u>Shares</u>	<u>Amount</u>						
<b>Balance December 31, 2001</b> .....	9,555,519	\$ 57	\$ 52,732	\$ —	\$ (39,235)	\$ —	\$ (60)	\$ 13,494
Proceeds from the issuance of common shares in connection with private placements, net.....	250,000	2	4,998	—	—	—	—	5,000
Proceeds from the exercise of options and warrants .....	388,187	2	2,172	—	—	—	60	2,234
Compensation related to stock options .....	—	—	2,604	(1,219)	—	—	—	1,385
Net loss.....	—	—	—	—	(13,468)	—	—	(13,468)
<b>Balance December 31, 2002</b> .....	10,193,706	61	62,506	(1,219)	(52,703)	—	—	8,645
Proceeds from the issuance of common shares and warrants in connection with private placement, net .....	1,513,069	9	9,954	—	—	—	—	9,963
Proceeds from the exercise of options .....	142,353	1	911	—	—	—	—	912
Compensation related to stock options .....	—	—	57	470	—	—	—	527
Net loss.....	—	—	—	—	(2,141)	—	—	(2,141)
<b>Balance December 31, 2003</b> .....	11,849,128	71	73,428	(749)	(54,844)	—	—	17,906
Proceeds from the issuance of common shares and warrants, net.....	5,386,364	32	65,144	—	—	—	—	65,176
Proceeds from the exercise of options and warrants .....	514,864	4	2,680	—	—	—	—	2,684
Compensation related to restricted stock .....	145,620	—	1,569	(1,081)	—	—	—	488
Compensation related to stock options .....	—	—	32	472	—	—	—	504
Net loss.....	—	—	—	—	(28,609)	—	—	(28,609)
Unrealized loss on securities available for sale .....	—	—	—	—	—	(1)	—	(1)
Comprehensive loss.....	—	—	—	—	—	(1)	—	(28,610)
<b>Balance December 31, 2004</b> .....	<u>17,895,976</u>	<u>\$ 107</u>	<u>\$ 142,853</u>	<u>\$ (1,358)</u>	<u>\$ (83,453)</u>	<u>\$ (1)</u>	<u>—</u>	<u>\$ 58,148</u>

See accompanying notes to consolidated financial statements.

**NASTECH PHARMACEUTICAL COMPANY INC. AND SUBSIDIARY**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(In Thousands)

	<u>Years Ended December 31,</u>		
	<u>2002</u>	<u>2003</u>	<u>2004</u>
<b>Operating activities:</b>			
Net loss .....	\$ (13,468)	\$ (2,141)	\$ (28,609)
Adjustments to reconcile net loss to net cash used in operating activities:			
Gain on sale of product .....	—	(4,236)	—
Non-cash compensation related to stock options .....	1,385	527	504
Non-cash compensation related to restricted stock .....	—	—	488
Depreciation and amortization of property and equipment .....	1,186	1,016	1,443
Amortization of intangible asset .....	216	398	—
Loss on retirement of property and equipment .....	—	—	35
Restructuring charge .....	595	—	—
Changes in assets and liabilities (net of assets sold in 2003):			
Accounts and other receivables .....	(543)	752	104
Inventories .....	(253)	102	123
Prepaid expenses and other current assets .....	(756)	(216)	215
Accounts payable .....	706	1,121	(738)
Deferred revenue .....	3,250	(3,250)	6,257
Accrued expenses and other liabilities .....	1,178	(1,759)	1,010
Net cash used in operating activities .....	<u>(6,504)</u>	<u>(7,686)</u>	<u>(19,168)</u>
<b>Investing activities:</b>			
Proceeds from sale of product .....	—	14,000	—
Purchases of investments .....	—	(13,689)	(46,589)
Maturities of investments .....	—	5,400	15,200
Purchase of license agreement .....	(1,457)	—	—
Property and equipment acquisitions .....	(2,363)	(2,229)	(2,164)
Net cash provided by (used in) investing activities .....	<u>(3,820)</u>	<u>3,482</u>	<u>(33,553)</u>
<b>Financing activities:</b>			
Sales of common shares and warrants, net .....	5,000	9,963	65,176
Restricted cash .....	—	(6,271)	(2,729)
Payments on notes payable .....	—	(7,979)	(146)
Proceeds from notes payable .....	—	7,000	2,227
Borrowings under capital lease obligations .....	401	2,443	1,885
Payments on capital lease obligations .....	(50)	(364)	(1,100)
Exercise of stock options and warrants .....	2,234	912	2,684
Net cash provided by financing activities .....	<u>7,585</u>	<u>5,704</u>	<u>67,997</u>
Net increase (decrease) in cash and cash equivalents .....	(2,739)	1,500	15,276
Cash and cash equivalents - beginning of year .....	11,760	9,021	10,521
Cash and cash equivalents - end of year .....	<u>\$ 9,021</u>	<u>\$ 10,521</u>	<u>\$ 25,797</u>
<b>Supplemental disclosures:</b>			
Cash paid for interest .....	\$ 26	\$ 518	\$ 414
<b>Non-cash investing and financing activities:</b>			
Purchase of license agreement financed by note payable .....	\$ 7,250	—	—
Net assets sold in connection with sale of product .....	—	\$ 6,534	—

See accompanying notes to consolidated financial statements.

**NASTECH PHARMACEUTICAL COMPANY INC. AND SUBSIDIARY**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**  
For the Three Years Ended December 31, 2004

**Note 1 — Business and Basis of Presentation**

***Business***

Nastech Pharmaceutical Company Inc. (“Nastech”, or the “Company”) is a pharmaceutical company focusing on development and commercialization of innovative products based on proprietary molecular biology-based intranasal drug delivery technology for delivering both small and large molecule drugs. Using this technology, the Company creates or utilizes novel formulation components or excipients that can transiently manipulate or open “tight junctions” between cells in various tissues and thereby allow therapeutic drugs to reach the blood stream. Tight junctions are cell-to-cell connections in various tissues of the body, including epithelial and endothelial layers of the intranasal mucosa, the gastrointestinal tract, and the blood brain barrier. They function to provide barrier integrity and to regulate the transport and passage of molecules across these natural boundaries. This technology is the foundation of the Company’s intranasal drug delivery platform, although some of the Company’s product candidates utilize this expertise outside this area. Generally, the Company seeks to apply its technology to compounds that the Company licenses to, or acquires from, collaborators or other third parties.

The Company believes its intranasal drug delivery technology offers advantages over injectable routes for the administration of large molecules such as peptides and proteins. These advantages may include improved safety and clinical efficacy and increased patient compliance due to the elimination of injection site pain and avoidance of injection site irritation. In addition, the Company believes its intranasal drug delivery technology offers advantages over oral administration by providing for faster absorption into the bloodstream, reduced side effects and improved effectiveness by avoiding problems relating to gastrointestinal and liver metabolism. The Company is utilizing its technologies to develop commercial products, initially with collaboration partners. In select cases, the Company also plans to internally develop, manufacture and commercialize its products.

The Company and its collaboration partners are developing a diverse portfolio of product candidates for multiple therapeutic areas including obesity, osteoporosis, breakthrough cancer pain, multiple sclerosis and erectile dysfunction. The Company’s lead product candidate, Peptide YY<sub>3-36</sub> (“PYY”) for obesity, is in Phase I clinical trials and is being developed with its collaboration partner, Merck & Co. Inc. (“Merck”). Additionally, the Company is developing two product candidates for the treatment of osteoporosis. Parathyroid Hormone (“PTH<sub>(1-34)</sub>”) is in Phase I clinical trials, and the Company has filed an abbreviated new drug application (“ANDA”) for its generic calcitonin-salmon intranasal spray which the Company is developing with its collaboration partner Par Pharmaceutical Inc. (“Par Pharmaceutical”). As of February 15, 2005, the Company has 41 patents issued and 161 patent applications filed to protect its proprietary technologies.

As of December 31, 2004, the Company has an accumulated deficit of approximately \$83.5 million and expects additional operating losses in the foreseeable future as it continues its research and development activities. The Company has funded its operating losses primarily through the sale of common stock in the public markets and private placements and also through revenues provided by its collaborative partners. During 2004, the Company received net proceeds of approximately \$65 million pursuant to two shelf registration statements, and at December 31, 2004 approximately \$33 million remains available on these shelf registration statements. At December 31, 2004, the Company has cash, cash equivalents and short-term investments of approximately \$74.5 million, including \$9.0 million in restricted cash.

The Company faces certain risks and uncertainties regarding its ability to generate positive operating cash flow and profits. These risks include, but are not limited to, its ability to obtain additional capital, protect its patents and property rights, overcome uncertainties regarding its technologies, competition and technological change, obtain government approval for products and attract and retain key officers and employees.

## **Note 2 — Summary of Significant Accounting Policies and Related Matters**

**Principles of Consolidation** - The financial statements include the accounts of Natestech Pharmaceutical Company Inc. and its wholly-owned subsidiary, Atossa HealthCare, Inc. ("Atossa"). All inter-company balances and transactions have been eliminated in consolidation. The Company operates in one segment and utilizes a platform of drug discovery technologies and development capabilities to discover and develop nasally administered formulations of prescription pharmaceuticals.

**Use of Estimates** - The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires the Company's management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, and reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

**Cash Equivalents** - Cash equivalents consist of cash, money market funds and investments in U.S. Government and Agency Securities and highly-rated investment grade commercial paper with maturities of 3 months or less at date of purchase.

**Restricted Cash** - Amounts pledged as collateral for notes payable are classified as restricted cash.

**Short term Investments** - Investments in marketable securities consist of debt instruments of U.S. government agencies and high quality corporate issuers (Standard & Poor's double "AA" rating and higher), have been categorized as available for sale and are stated at fair value. Unrealized holding gains and losses on available-for-sale securities are excluded from earnings and are reported as a separate component of other comprehensive income until realized. Realized gains and losses from the sale of available-for-sale securities are determined on a specific-identification basis. A decline in the market value of any available-for-sale security that is deemed to be other-than-temporary results in a reduction in carrying amount to fair value. The impairment is charged to earnings and a new cost basis for the security is established. To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. Evidence considered in this assessment includes the reasons for the impairment, the severity and duration of the impairment, changes in value subsequent to year-end and forecasted performance of the investee. Premiums and discounts are amortized or accreted over the life of the related available-for-sale security as an adjustment to yield using the effective-interest method. Dividend and interest income are recognized when earned.

**Inventories** - Inventories are stated at the lower of cost (first-in, first-out basis) or market and consist of raw materials.

**Intangible Assets and Goodwill** - Intangible assets consisted of costs associated with the purchase of a license agreement related to the Nascobal® product. Such costs were being amortized over a ten-year period from the date of acquisition using the straight-line method at \$864,000 per year. In June 2003, the Company completed the sale of certain assets relating to the Nascobal® brand products to Questcor Pharmaceuticals, Inc. ("Questcor"), at which time the intangible asset was sold. Amortization expense recorded in 2002, 2003 and 2004 was \$216,000, \$398,000 and zero, respectively.

Goodwill represents the cost in excess of the net assets resulting from the Company's acquisition in 2000 of Atossa. Until December 31, 2001, goodwill was amortized on a straight-line basis over a three-year period. In accordance with SFAS 142, *Goodwill and Other Intangible Assets* ("SFAS 142") this amortization ceased after December 31, 2001. The total goodwill resulting from the Atossa acquisition was \$171,000, and accumulated amortization at December 31, 2001 was \$81,000. Goodwill is evaluated for possible impairment at least annually, most recently at December 31, 2004, and whenever significant events or changes in circumstances, including changes in the Company's business strategy and plans, indicate that an impairment may have occurred. Amortization expense recorded in 2000 and 2001 was \$24,000 and \$57,000, respectively.



As a result of the Company's research and development programs ("R&D"), the Company has applied for a number of patents in the United States and abroad. Such patent rights are of significant importance to the Company to protect products and processes developed. Costs incurred in connection with patent applications for the Company's R&D program have been expensed as general and administrative expenses as incurred.

**Property and Equipment** - Property and equipment are stated at cost and depreciated using straight-line methods over estimated useful lives ranging from three to ten years. Leasehold improvements are stated at cost and amortized using the straight-line method over the lesser of the estimated useful life or the remaining lease term. When assets are sold or retired, the cost and related accumulated depreciation are removed from the accounts and any resulting gain or loss is recognized. Expenditures for maintenance and repairs are charged to expense as incurred.

**Impairment of long-lived assets** - Long-lived assets, including property and equipment, are evaluated for possible impairment whenever significant events or changes in circumstances, including changes in the Company's business strategy and plans, indicate that an impairment may have occurred. The company evaluates the carrying value of the asset by comparing the estimated future undiscounted net cash flows to its carrying value. If the net carrying value exceeds the future undiscounted net cash flows, impairment losses are determined from actual or estimated fair values, which are based on market values, net realizable values or projections of discounted net cash flows, as appropriate.

**Revenue Recognition** - Most of the Company's revenues are generated from research and licensing arrangements. These research and licensing arrangements may include upfront non-refundable payments, development milestone payments, revenue from product manufacturing, payments for research and development services performed and product sales royalties or revenue. The Company's revenue recognition policies are based on the requirements of Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 104 "Revenue Recognition," and, for contracts with multiple deliverables, the Company determines the appropriateness of separate units of accounting and allocates arrangement consideration based on the fair value of the elements under guidance from Emerging Issues Task Force Issue 00-21 ("EITF 00-21"), "Revenue Arrangements with Multiple Deliverables." Under EITF 00-21, revenue arrangements with multiple deliverables are divided into separate units of accounting such as product development and contract manufacturing. Revenue is allocated to these units based upon relative fair values with revenue recognition criteria considered separately for each unit.

Nonrefundable upfront technology license fees, for product candidates where we are providing continuing services related to product development, are deferred and recognized as revenue over the development period or as the Company provides the services required under the agreement. The ability to estimate total development effort and costs can vary significantly for each product candidate due to the inherent complexities and uncertainties of drug development.

Milestones, in the form of additional license fees, typically represent nonrefundable payments to be received in conjunction with the achievement of a specific event identified in the contract, such as initiation or completion of specified clinical development activities. The Company believes that a milestone represents the culmination of a distinct earnings process when it is not associated with ongoing research, development or other performance on the Company's part. The Company recognizes such milestones as revenue when they become due and collection is reasonably assured. When a milestone does not represent the culmination of a distinct earnings process, revenue is recognized in manner similar to that of an upfront technology license fee.

The timing and amount of revenue that the Company recognizes from licenses of technology, either from upfront fees or milestones where the Company is providing continuing services related to product development, is dependent upon on the Company's estimates of filing dates or development costs. As product candidates move through the development process, it is necessary to revise these estimates to consider changes to the product development cycle, such as changes in the clinical development plan, regulatory requirements, or various other factors, many of which may be outside of the Company's control. The impact on revenue of changes in the

Company's estimates and the timing thereof, is recognized prospectively, over the remaining estimated product development period.

Royalty revenue is generally recognized at the time of product sale by the licensee.

Revenue from research and development services performed is generally received for services performed under collaboration agreements, and is recognized at the time the services are performed. Payments received in excess of amounts earned are recorded as deferred revenue.

Product sales revenue is recognized at the time the manufactured goods are shipped to the purchaser and title has transferred.

For the year ended December 31, 2002, a substantial portion of revenue was derived from upfront fees, milestone payments and revenue from R&D services performed for Pharmacia & Upjohn Company ("Pharmacia") and from direct sales of Nascobal® nasal gel. For the year ended December 31, 2003, a substantial portion of revenue was derived from revenue recognized as a result of payments received by the Company as a result of the divestiture agreement entered into with Pharmacia. For the year ended December 31, 2004, revenue was primarily derived from amortization of license fees received from Merck and Par Pharmaceutical, research and development services performed for Merck and other collaboration partners and Nascobal® nasal gel sales to Questcor.

**Net Loss per Common Share** - Basic and diluted net loss per common share is computed by dividing the net loss by the weighted average number of common shares outstanding during the period. Basic loss per share excludes the effect of unvested restricted shares in 2004 of 145,620 shares. Diluted loss per share excludes the effect of common stock equivalents (stock options, unvested restricted stock and warrants) since such inclusion in the computation would be anti-dilutive. Such excluded stock options, restricted stock and warrants amounted to 3,432,752 shares in 2002, 4,109,302 shares in 2003 and 4,390,944 shares in 2004.

**Income Taxes** - Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carry-forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

**Stock-Based Compensation** - The Company accounts for stock-based compensation using the intrinsic value method in accordance with APB No. 25, *Accounting for Stock Issued to Employees* ("APB 25"). Under APB 25, when stock options are issued with an exercise price equal to the market price of the underlying stock price on the date of grant, no compensation expense is recognized. The Company continues to follow the disclosure-only provisions of SFAS No. 123, *Accounting for Stock-Based Compensation* ("SFAS 123"), which requires the disclosure of pro forma net income and earnings per share as if the Company had applied the fair value recognition provisions of SFAS 123.

The per share weighted average fair value of stock options granted during the fiscal years ended December 31, 2002, 2003 and 2004 was \$9.53, \$6.02 and \$7.75, respectively, on the date of grant using the Black Scholes option-pricing model with the following assumptions:

	Years Ended December 31,		
	2002	2003	2004
Expected dividend yield .....	0%	0%	0%
Risk free interest rate .....	3.8%	3.0%	3.4%
Expected stock volatility .....	96%	89%	78%
Expected option life .....	5 years	5 years	5 years

Had the Company determined compensation cost based on the fair value at the grant date for its stock options under SFAS No. 123, its net loss would have been reported as the pro forma amounts indicated below:

	Years Ended December 31,		
	(in thousands, except per share amounts)		
	2002	2003	2004
Net loss, as reported.....	\$ (13,468)	\$ (2,141)	\$ (28,609)
Add: stock-based employee compensation included in the reported net loss.....	1,385	527	992
Deduct: stock-based employee compensation, determined under fair value based methods.....	(6,965)	(5,537)	(5,585)
Pro forma net loss.....	<u>\$ (19,048)</u>	<u>\$ (7,151)</u>	<u>\$ (33,202)</u>
Loss per share:.....			
Basic and diluted – as reported.....	\$ (1.34)	\$ (0.20)	\$ (2.21)
Basic and diluted – pro forma.....	\$ (1.90)	\$ (0.67)	\$ (2.56)

**Research and Development Costs** - All R&D costs are charged to operations as incurred. The Company's R&D expenses consist of costs incurred for internal and external research and development. These costs include direct and research-related overhead expenses.

**Shipping and Handling Costs** - Costs of shipping and handling for delivery of the Company's products that are reimbursed by its customers are recorded as revenue in the statement of operations. Shipping and handling costs are charged to cost of goods sold as incurred.

**Advertising Costs** - Advertising costs are expensed as incurred and are included in sales and marketing expense. For the years ended December 31, 2002, 2003 and 2004, total advertising expense was approximately \$282,000, \$11,000 and \$9,000, respectively.

**Other Comprehensive Income or Loss** - In the year ended December 31, 2004, the only component of other comprehensive loss was unrealized losses on securities in the amount of \$1,000. There were no components of other comprehensive income (loss) in the years ended December 31, 2002 and December 31, 2003.

**Fair Value of Financial Instruments** - The Company considers the fair value of all financial instruments to not be materially different from their carrying value at year-end as all financial instruments have short-term maturities.

**Reclassifications** - Certain reclassifications have been made to prior years' financial statements to conform with current year presentations. Such reclassifications had no effect on stockholders' equity or net loss.

**Recent Accounting Pronouncements** - In November 2004, the FASB issued SFAS 151 ("SFAS 151"), *Inventory Costs, an amendment of ARB No. 43, Chapter 4*. The standard requires that abnormal amounts of idle capacity and spoilage costs should be excluded from the cost of inventory and expensed when incurred. The provision is effective for fiscal periods beginning after June 15, 2005. The Company does not expect the adoption of this standard to have a material effect on the Company's consolidated financial statements.

In December 2004, the FASB issued SFAS 153 ("SFAS 153"), *Exchanges of Nonmonetary Assets, an amendment of APB No. 29, Accounting for Nonmonetary Transactions*. SFAS 153 requires exchanges of productive assets to be accounted for at fair value, rather than at carryover basis, unless (1) neither the asset received nor the asset surrendered has a fair value that is determinable within reasonable limits or (2) the transactions lack commercial substance. SFAS 153 is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. The Company does not expect the adoption of this standard to have a material effect on the Company's consolidated financial statements.

In December 2004, the FASB released its revised standard, SFAS No. 123R (SFAS 123R"), *Share-Based Payment*. SFAS 123R requires that a public entity measure the cost of equity based service awards based on the

grant-date fair value of the award. That cost will be recognized over the period during which an employee is required to provide service in exchange for the award or the vesting period. A public entity will initially measure the cost of liability based service awards based on its current fair value and the fair value of that award will be remeasured subsequently at each reporting date through the settlement date. Changes in fair value during the requisite service period will be recognized as compensation cost over that period. Adoption of SFAS 123R is required for fiscal periods beginning after June 15, 2005. The Company is evaluating SFAS 123R and believes it will likely result in recognition of additional non-cash stock-based compensation expense and accordingly would increase net loss in amounts which likely will be considered material.

### Note 3 — Short-term investments

Short-term investments consisted of the following (in thousands):

<u>December 31, 2003</u>	<u>Amortized cost</u>	<u>Gross unrealized gain</u>	<u>Gross unrealized loss</u>	<u>Estimated Fair Value</u>
Type of security:				
Commercial Paper and Money Market .....	\$ 1,016	-	\$ (1)	\$ 1,015
US Government and Agency Securities .....	7,273	\$ 1	-	7,274
Total.....	<u>\$ 8,289</u>	<u>\$ 1</u>	<u>\$ (1)</u>	<u>\$ 8,289</u>

<u>December 31, 2004</u>	<u>Amortized cost</u>	<u>Gross unrealized gain</u>	<u>Gross unrealized loss</u>	<u>Estimated Fair Value</u>
Type of security:				
Commercial Paper and Money Market .....	\$ 997	—	—	\$ 997
US Government and Agency Securities .....	4,633	—	\$ (1)	4,632
Auction Rate Notes .....	34,048	—	—	34,048
Total.....	<u>\$ 39,678</u>	<u>—</u>	<u>\$ (1)</u>	<u>\$ 39,677</u>

The Company has concluded that unrealized losses are temporary due to the ability of the Company to realize the full value of its investments at maturity. Such unrealized losses have existed for less than 12 months.

### Note 4 — Property and Equipment

Property and equipment at December 31, 2003 and 2004 are comprised of (in thousands):

	<u>2003</u>	<u>2004</u>
Furniture and fixtures .....	\$ 619	\$ 564
Machinery and equipment .....	4,614	4,822
Computer equipment .....	1,295	1,523
Leasehold improvements .....	<u>1,763</u>	<u>1,871</u>
	8,291	8,780
Less accumulated depreciation and amortization .....	<u>3,817</u>	<u>3,620</u>
Net property and equipment .....	<u>\$ 4,474</u>	<u>\$ 5,160</u>

Assets under capital lease, primarily equipment, totaled \$2.8 million and \$4.7 million at December 31, 2003 and 2004, respectively, and accumulated amortization of capital leases totaled \$0.5 million and \$1.3 million at December 31, 2003 and 2004, respectively.

## Note 5 — Accrued Expenses

Accrued expenses at December 31, 2003 and 2004 are comprised of (in thousands):

	2003	2004
Accrued payroll and employee benefits.....	\$ 1,060	\$ 1,469
Allowance for sales returns .....	165	138
Interest payable.....	12	24
Audit and tax services.....	66	89
Legal fees.....	27	20
Other accrued expenses .....	180	793
	<u>\$ 1,510</u>	<u>\$ 2,533</u>

## Note 6 — Employee Benefit Plan

The Company has a 401(k) plan for those employees who meet eligibility requirements. Eligible employees may contribute up to 100% of their eligible compensation, subject to IRS limitations. Company contributions to the plans are discretionary as determined by the Company's Board of Directors ("the Board"). Effective January 1, 2004, the Company implemented a matching program to match employee contributions of up to 6% of compensation at 25 cents for each dollar contributed by the employee. Employer contributions in each of the years ended December 31, 2002 and December 31, 2003 were zero, and were \$79,000 in the year ended December 31, 2004.

## Note 7 — Purchase and Sale of Nascobal Assets

The Company entered into a License and Supply Agreement on July 15, 1997, with Schwarz Pharma, Inc. ("Schwarz Pharma") whereby Schwarz Pharma agreed to promote, market, sell and distribute the Company's product, Nascobal® nasal gel (the "Schwarz Pharma Agreement"). The Company retained worldwide manufacturing rights and the right to sell this product to other future licensees outside the U.S. There have been no foreign sales or any upfront or milestone payments to date. Pursuant to the Schwarz Pharma Agreement, the Company received royalty payments from Schwarz Pharma based upon the net sales of Nascobal® nasal gel. The Company also recorded product sales revenues each time Schwarz Pharma purchased Nascobal® nasal gel. The Company received aggregate sales and royalty payments under the Schwarz Pharma Agreement of \$493,000 in 2002. This agreement terminated in September 2002 as discussed below.

In September 2002, the Company purchased Schwarz Pharma's rights, title and interests arising under or by virtue of the Schwarz Pharma Agreement (the "Acquisition Agreement"). Under the Acquisition Agreement, Schwarz Pharma relinquished its rights to receive any consideration from the Company from a second-generation dosage form of Nascobal® as well as any consideration upon the future sale or license of intranasal scopolamine. Cancellation of the scopolamine agreement relieved the Company of a contingent liability of approximately \$4.0 million.

The transaction was accounted for as an asset purchase. Under terms of the Acquisition Agreement, the Company agreed to pay Schwarz Pharma a total of \$8.75 million. Costs associated with the transaction were approximately \$78,000. The \$8.87 million valuation of Schwarz Pharma's rights, title and interests arising under or by virtue of the Schwarz Pharma Agreement was based on management's estimates using a valuation report prepared by an independent third-party valuation consultant and consists of the Schwarz Pharma Agreement. Prior to the 2003 sale to Questcor as described below, the Company was amortizing the purchase price over a ten-year period, which represented the estimated economic life of the product.

The Company made an upfront payment of \$1.5 million to Schwarz Pharma at the closing in September 2002, with the remaining balance of \$7.25 million evidenced by a note payable issued to Schwarz Pharma. The note was to be repaid in semi-annual installments over a four-year period plus interest at 7.50% per annum on any outstanding balance. The Company granted a security interest to Schwarz Pharma in certain assets that relate specifically to Nascobal, including, without limitation, patents, trademarks, copyrights, licenses and permits, inventory, receivables

and manufacturing equipment. Under the terms of the note, the Company made a payment of \$654,000 to Schwarz Pharma in March 2003, which was comprised of \$382,000 in principal on the note and \$272,000 of accrued interest.

The Company and Schwarz Pharma share the financial liability for return of Nascobal® nasal gel units sold by Schwarz Pharma prior to September 30, 2002. Schwarz Pharma is responsible for 84% and Natestch 16% of the aggregate value of all returns with an aggregate value of up to \$379,000. The Company's contingent liability under this arrangement was \$60,640, which was recorded as an increase in the purchase price of the asset. Natestch is responsible for all returns in excess of \$379,000 in the aggregate. Through December 31, 2004 Schwarz Pharma returns have approximated \$276,000.

In addition, in October 2002, the Company purchased the remaining units of Nascobal® nasal gel inventory from Schwarz Pharma for \$136,000, its original purchase price of such inventory from the Company. The inventory was recorded in 2002 at fair value totaling \$319,000 in accordance with purchase accounting rules.

In June 2003, the Company entered into an agreement to sell Nascobal to Questcor. In connection with the sale, the remaining \$6.9 million note payable to Schwarz Pharma and accrued interest of approximately \$110,000 were paid in full. Schwarz Pharma subsequently released its security interest in certain assets that relate specifically to Nascobal, including, without limitation, patents, trademarks, copyrights, licenses and permits, inventory, receivables and manufacturing equipment. Under the terms of a supply agreement with Questcor, subject to certain limitations, the Company is obligated to manufacture and supply all of Questcor's requirements and Questcor is obligated to purchase from us all of its requirements for the Nascobal® nasal gel and the Nascobal® nasal spray upon FDA's final approval. The Company has filed the NDA and will continue to prosecute the pending U.S. patents for the Nascobal® nasal spray product on behalf of Questcor. In February 2005, Questcor paid a milestone fee to the Company of \$2.0 million upon final FDA approval of the NDA for the Nascobal® nasal spray, and has agreed to pay an additional \$2.0 million contingent upon issuance of a U.S. patent for the Nascobal® nasal spray.

#### **Note 8 — Notes Payable**

In June 2003, the Company issued a cash secured Revolving Reducing Note to Wells Fargo Bank (the "Wells Fargo Note"). Under terms of the Wells Fargo Note, the Company could borrow up to \$7.0 million for a one-year term and fix the interest rate for one, two or three months at a rate of 0.75% above LIBOR. If the interest rate and term are not fixed, the interest rate will be 1.5% below prime. Interest accrued on the note is due monthly on the first day of the following month. The amount available under the note decreased by approximately \$146,000 per month as of the first day of each month and the Company was required to make a principal payment on the first day of the month in an amount sufficient to reduce the then outstanding principal balance to the new maximum principal amount available.

In December 2003, the Company terminated the June 2003 Wells Fargo Note and issued a new cash secured Revolving Line of Credit Note to Wells Fargo Bank to allow for borrowings up to \$9.0 million through December 31, 2004. Monthly principal payments are no longer required under the new note and the interest rate and monthly interest payments are the same as the original note. The entire balance of the note was due December 31, 2004. In January, 2004, the Revolving Line of Credit Note was amended to incorporate a Letter of Credit Subfeature (the "Subfeature"). Under the Subfeature, approximately \$648,000 of the \$9.0 million line of credit was reserved for issuance of a standby letter of credit agreement to the Company's landlord for its Bothell, Washington operations under the terms of its facility lease.

In October 2004 the Company renewed and increased the Revolving Line of Credit Note (the "Credit Agreement") to allow for borrowings up to \$11.5 million through December 31, 2005. The Subfeature was increased to \$1.0 million. The entire balance of the note is due December 31, 2005. As of December 31, 2004, the interest rate was fixed for a 90 day term at 3.25% on borrowings of approximately \$8,352,000. On February 1, 2005, the Letter of Credit issued to the Company's landlord was increased to approximately \$998,000 under the terms of its facility lease. Pursuant to terms of the Credit Agreement, the Company has, among other things, agreed not to incur additional indebtedness or pay dividends.

On February 18, 2005, the Company paid off the Credit Agreement borrowings of \$8,352,000.

#### **Note 9 — Stockholders' Equity**

**Common Stock Offerings** - In a 2001 private offering, the Company granted warrants to purchase 68,000 shares of its common stock at any time prior to May 11, 2005, at an exercise price of \$7.50 per share of common stock. As of December 31, 2004, 65,900 warrants relating to this private placement have been exercised. In connection with such private placement, the Company granted additional warrants to purchase 595,155 shares of its common stock, which warrants are exercisable at any time prior to March 22, 2006 at an exercise price of \$6.34 per share. As of December 31, 2004, 103,977 warrants issued in connection with these private placements have been exercised.

In March 2002, the Company sold 250,000 shares of common stock for \$5 million in cash to Pharmacia at \$20.00 per share in conjunction with the February 2002 Collaboration and License Agreement between the Company and Pharmacia.

In September 2003, the Company completed the sale of 1,513,069 units, each unit consisting of one share of common stock, par value \$0.006 per share, and one five year warrant convertible into 0.35 common shares, to certain accredited investors in a private placement transaction for an aggregate purchase price of \$11 million, prior to the deduction of fees and commissions totaling \$1,037,000. The units were sold at \$7.27 per unit, which was an 18% discount from the volume weighted average price for the 10 days prior to the completion of the private placement transaction. The warrants are exercisable for 529,574 shares of common stock at an exercise price per share of \$11.09, subject to adjustment from time to time for stock splits, stock dividends, distributions or similar transactions. The warrants expire in September 2008. At December 31, 2004, 48,143 warrants issued in connection with this private placement have been exercised.

In June 2004, the Company completed the sale of 1,136,364 shares of its common stock, and warrants to purchase up to 511,364 shares of common stock at an exercise price of \$14.40 per share, pursuant to its \$30 million effective shelf registration statement. The offering resulted in gross proceeds of approximately \$12.5 million to the Company prior to the deduction of fees and commissions of \$229,000. The warrants vested on December 25, 2004, and are exercisable until June 25, 2009. At December 31, 2004, the amount remaining available on this shelf registration statement was approximately \$10.1 million. At December 31, 2004, no warrants issued in connection with this private placement have been exercised.

In December 2004, the Company completed the public offering of 4,250,000 shares of its common stock at a public offering price of \$13.50 per share pursuant to its \$80 million effective shelf registration statement. The offering resulted in gross proceeds of approximately \$57.4 million to the Company, prior to the deduction of fees and commissions of \$4.5 million.

**Restricted Stock Awards** - Pursuant to certain restricted stock awards granted pursuant to the Company's 2004 Stock Incentive Plan, in 2004 the Company granted and issued approximately 146,000 shares of restricted common stock to certain employees and members of the Board. Non-cash compensation expense is being recognized on a straight-line basis over the applicable vesting periods of one to three years of the restricted shares based on the fair value of such common stock on the grant date, which approximated \$1.6 million in deferred compensation. The Company expensed approximately \$0.5 million as stock compensation expense related to this program during the year ended December 31, 2004.

**Shelf Registration Statements** - The Company currently has two effective shelf registration statements on Form S-3. On December 18, 2003, the Company filed a shelf registration statement with the SEC, which was declared effective by the SEC on January 14, 2004, pursuant to which it may issue common stock or warrants, up to an aggregate of \$30 million. On September 30, 2004 the Company filed another shelf registration statement with the SEC, which was declared effective by the SEC on October 8, 2004, pursuant to which it may issue common stock, warrants or debt securities, up to an aggregate of \$80 million. These shelf registration statements enable the Company to raise

capital from the offering of securities covered by the shelf registration statements, as well as any combination thereof, from time to time and through one or more methods of distribution, subject to market conditions and cash needs.

**Stockholders' Rights Plan** - In 2000, the Company enacted a stockholder rights plan designed to protect its stockholders from coercive or unfair takeover tactics. Under the plan, the Company declared a dividend of one preferred stock purchase right for each share of common stock and entered into a Rights Agreement with the Company's stock transfer agent. Each preferred stock purchase right entitles the holder to purchase from the Company 1/1000 of a share of its Series A Junior Participating Preferred Stock for \$50. In the event any acquiring entity or group accumulates or initiates a tender offer to purchase 15% or more of the Company's common stock, then each holder of the Company's common stock shall receive a separate certificate evidencing the rights (the "Rights Distribution"). Each preferred stock purchase right, other than the acquiring entity, will have the right to receive, upon exercise of the preferred stock purchase right, shares of the Company's common stock or shares in the acquiring entity having a value equal to two times the exercise price of the preferred stock purchase right.

#### **Note 10 — Stock Options**

In June 2004, the Company established the 2004 Stock Incentive Plan (the "2004 Plan") under which a total of 600,000 shares have been reserved for issuance. As of December 31, 2004, 145,620 shares of restricted common stock were outstanding under the 2004 Plan which vest between one and three years and 454,380 authorized shares were available for future issuance. The average grant date fair value of the restricted shares granted in 2004 was \$9.39.

In 2002, the Company established the 2002 Stock Option Plan, pursuant to which options to purchase an aggregate of 1,362,500 shares of common stock were outstanding and 37,500 authorized shares were available for future issuance as of December 31, 2004.

In 2000, the Company established the 2000 Nonqualified Stock Option Plan, pursuant to which options to purchase an aggregate of 664,533 shares of common stock were outstanding and 126,990 authorized shares were available for future issuance as of December 31, 2004.

In 1990, the Company established the 1990 Stock Option Plan, pursuant to which options to purchase an aggregate of 260,500 shares of common stock were outstanding under the 1990 Plan and no shares were available for future issuance as of December 31, 2004.

In addition, in 2002 the Company approved and ratified the issuance of 561,719 stock options outside the plans to certain executive officers in connection with the commencement of their employment with the Company.

The Company has filed separate registration statements on Form S-8 registering awards under each of the Company's equity compensation plans and the 561,719 options awarded outside the plans.

Under its 1990, 2000 and 2002 stock compensation plans, the Company is authorized to grant options to purchase shares of common stock to its employees, officers and directors and other persons who provide services to the Company. The options to be granted are designated as either incentive stock options or non-incentive stock options by the Board, which also has discretion as to the person to be granted options, the number of shares subject to the options and the terms of the option agreements. Only employees, including officers and part-time employees, may be granted incentive stock options. Under its 2004 Stock Incentive Plan, the Company is authorized to grant awards of restricted stock, stock appreciation rights and performance shares, in addition to stock options. As of December 31, 2004, the Company had only granted restricted stock awards from this plan.

The plans provide that options granted there under shall be exercisable during a period of no more than ten years (five years in the case of 10% shareholders) from the date of grant, depending upon the specific stock option agreement, and that, with respect to incentive stock options, the option exercise price shall be at least equal to 100%



of the fair market value of the common stock at the time of grant (110% in the case of 10% shareholders). Pursuant to the provisions of the stock option plans, the aggregate fair market value (determined on the date of grant) of the common stock with respect to which incentive stock options are exercisable for the first time by an employee during any calendar year shall not exceed \$100,000.

On May 2, 2002, the Company extended the term of the employment agreement of its chief executive officer ("CEO") through December 31, 2005. In connection with the extension, the Company granted its CEO an option to purchase 800,000 shares of common stock at an exercise price of \$12.94 per share, which was the market price at the date of grant. The option vests as follows: 200,000 options immediately and 200,000 options each in August 2003, August 2004 and August 2005. The Company's stockholders approved the option plan that included the CEO options on June 6, 2002 when the stock price was \$15.43 per share. The change in price between the date of grant and the date the plan was approved by the stockholders resulted in deferred stock-based compensation expense of \$2.0 million that is being recognized as expense on a straight-line basis over the vesting period. For the years ended December 31, 2002, 2003 and 2004, the Company recognized expense of approximately \$773,000, \$470,000 and \$472,000, respectively.

In October 2002, the Board, in order to allow for a more orderly distribution of shares on the market, voted in favor of extending the expiration date for options held by certain members of the Board expiring in June or August 2003 to 10 years after the date of the original grant. Directors who did not hold any affected options unanimously approved these changes. The new option expiration dates are in June 2005 and August 2008, respectively. A related charge of approximately \$612,000 was recorded in general & administrative expense in 2002.

As of December 31, 2004, the Company had 164,490 shares of common stock available for future grant under its 2000 and 2002 stock option plans. In addition, the Company issued 561,719 stock options outside the plans in 2002. These shares are included in the table below. Data relating to the stock options issued are as follows:

	2002		Years Ended December 31, 2003		2004	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of period.....	1,897,876	\$ 6.66	2,863,574	\$ 10.34	3,010,550	\$ 10.43
Granted .....	1,417,100	13.80	644,800	8.91	215,500	11.37
Exercised .....	(404,340)	5.28	(142,353)	7.24	(430,132)	5.09
Expired .....	—	—	(48,569)	8.31	(667)	12.43
Terminated and canceled .....	(47,062)	10.22	(306,902)	8.61	(35,999)	8.77
Outstanding at end of period.....	<u>2,863,574</u>	<u>\$ 10.34</u>	<u>3,010,550</u>	<u>\$ 10.43</u>	<u>2,759,252</u>	<u>\$ 11.36</u>

The following table summarizes additional information on the Company's stock options outstanding at December 31, 2004:

Range of exercise prices	Number outstanding	Options Outstanding		Options Exercisable	
		Weighted-average remaining contractual life (years)	Weighted-average exercise price	Number exercisable	Weighted-average exercisable price
\$4.09 - \$5.62....	407,619	1.4	\$ 4.77	407,619	\$ 4.77
\$7.00 - \$8.25....	197,866	4.0	8.10	98,237	8.15
\$8.33 - \$9.99....	294,967	6.3	9.21	106,773	9.12
\$10.24 -	326,000	6.0	10.82	184,935	10.67
\$11.24 .....					
\$12.00 -	1,027,000	5.9	12.74	810,667	12.70
\$12.94 .....					
\$13.06 -	122,800	4.2	13.58	46,668	13.35
\$13.92 .....					
\$15.00 -	283,000	1.6	15.23	238,668	15.21
\$16.00 .....					
\$25.00 .....	100,000	7.3	25.00	—	—
Totals .....	<u>2,759,252</u>	<u>4.7</u>	<u>\$ 11.36</u>	<u>1,893,567</u>	<u>\$ 10.69</u>

## Note 11 — Income Taxes

The Company's net deferred tax assets as of December 31, 2003 and 2004 are estimated as follows (in thousands):

	<u>2003</u>	<u>2004</u>
Deferred tax assets:		
Net operating loss carryforwards .....	\$ 18,631	\$ 26,423
Federal and State tax credits .....	2,182	3,496
Depreciation & amortization .....	1,328	959
Deferred revenue .....	—	2,190
Other .....	564	2,042
Total deferred tax assets .....	\$ 22,705	\$ 35,110
Valuation allowance .....	(22,705)	(35,110)
Net deferred taxes .....	<u>—</u>	<u>—</u>

The Company continues to record a valuation allowance in the full amount of deferred tax assets since realization of such tax benefits is not considered to be more likely than not. The valuation allowance increased \$6.2 million, \$0.3 million and \$12.4 million during 2002, 2003 and 2004, respectively. As a result of the valuation allowance, there was no tax benefit or expense recorded in the accompanying statement of operations for the years ended December 31, 2002, 2003 or 2004, respectively.

At December 31, 2004, the Company had available net operating loss carryforwards for federal and state income tax reporting purposes of approximately \$69.4 million and \$27.7 million, respectively, and has available tax credits of approximately \$3.5 million, which are available to offset future taxable income. These carryforwards will begin to expire in 2005 and will continue to expire through 2024 if not otherwise utilized. The Company's ability to use such net operating loss and federal and state tax credit carryforwards may be limited by change of control provisions under Sections 382 and 383 of the Internal Revenue Code.

During 2002, 2003 and 2004, employee stock options were exercised that resulted in income tax deductions in the amount of approximately \$1.7 million, \$0.3 million, and \$2.9 million, respectively. The cumulative total of such deductions at December 31, 2004 is approximately \$5.9 million, and such amount is included in the Company's available net operating loss carryforwards as of December 31, 2004. Excess tax benefit relating to such stock options will be credited to additional paid-in capital in the period the related tax deduction is realized.

The difference between the expected benefit computed using the statutory tax rate and the recorded benefit of \$0 is due to the change in the valuation allowance.

## Note 12 — Lease Commitments and restructuring charge

The Company leases space for its manufacturing, research and development and corporate offices in Bothell, Washington under a lease expiring in January 2016 and for manufacturing and research and development activities in Hauppauge, New York under a lease expiring on June 30, 2005.

Rental expense aggregated approximately \$0.8 million, \$1.4 million, and \$1.5 million, for the years ended December 31, 2002, 2003 and 2004, respectively.

The following is a schedule of future annual minimum lease payments under the facility leases and capital leases as of December 31, 2004 (in thousands):

	Facility leases	Capital leases	Total
2005 .....	\$ 1,661	\$ 1,753	\$ 3,414
2006 .....	1,655	1,380	3,035
2007 .....	1,696	449	2,145
2008 .....	1,738	—	1,738
2009 .....	1,782	—	1,782
Thereafter .....	11,841	—	11,841
Less amount representing interest .....	—	(331)	(331)
Total .....	<u>\$ 20,373</u>	<u>\$ 3,251</u>	<u>\$ 23,624</u>

In addition, the Company also leased space in Hauppauge, New York for R&D and administrative activities under a lease expiring October 31, 2009 (“Adams Avenue Facility”). In February 2003, the Company executed a lease termination agreement for this facility, together with a sublease for a portion of the facility through December 31, 2003. As a result, the Company recorded a restructuring charge in 2002 in the amount of approximately \$595,000, which was comprised of the write-off of Adams Avenue Facility unamortized leasehold improvements of approximately \$871,000 and site preparation costs of \$86,000, which were offset by the elimination of the deferred rent liability of \$362,000.

### **Note 13 — Contractual Agreements**

**Merck.** - In September 2004, the Company entered into an Exclusive Development, Commercialization and License Agreement and a separate Supply Agreement (collectively, the “Agreements”) with Merck, for the global development and commercialization of PYY Nasal Spray, the Company’s Phase I product for the treatment of obesity. The Agreements provide that Merck will assume primary responsibility for conducting and funding clinical and non-clinical studies and regulatory approval, while the Company will be responsible for all manufacturing of PYY-related product. Merck will lead and fund commercialization, subject to the Company’s exercise of an option to co-promote the product in the United States.

Under the Agreements, the Company received an initial cash payment of \$5 million in 2004. The \$5 million initial payment is being amortized over the estimated development period, and has been recorded as deferred revenue in the accompanying balance sheet. If certain development and approval milestones are achieved, the Company will be eligible to receive up to an additional \$131 million from Merck. If certain sales-related milestones are achieved, the Company would be eligible to receive up to an additional \$210 million from Merck subject to certain other conditions. Merck will pay the Company for manufacturing-related development activities and will purchase all clinical supply and finished product upon commercialization from the Company. The Company will also receive royalties on product sales.

**Thiakis Limited** - In September 2004, the Company announced it acquired exclusive worldwide rights to the Imperial College Innovations and Oregon Health & Science University PYY patent applications in the field of intranasal delivery of PYY and the use of glucagons-like peptide-1 (GLP-1) used in conjunction with PYY for the treatment of obesity, diabetes and other metabolic conditions. Under the agreement, Nastech made an equity investment in and paid an initial license fee to Thiakis, Ltd. (“Thiakis”). The equity investment and initial license fee were expensed as research and development expenses by the Company in 2004. Under the agreement, Thiakis is entitled to receive an annual fee, additional milestone fees, patent-based royalties, and additional equity investments based upon future progress of the intellectual property and product development processes.

**Par Pharmaceutical** - In October 2004, the Company entered into a license and supply agreement with Par Pharmaceutical for the exclusive U.S. distribution and marketing rights to its generic calcitonin-salmon nasal spray. Under the terms of the agreement with Par Pharmaceutical, the Company will manufacture and supply finished generic calcitonin-salmon nasal spray product to Par Pharmaceutical, while Par Pharmaceutical will distribute the product in the US. The financial terms of the agreement include milestone payments, product transfer payments for

manufactured product and a profit sharing following commercialization. The Company filed its ANDA with the FDA in December 2003, which was accepted in February 2004.

**Questcor** - In June 2003, the Company completed the sale of certain assets relating to its Nascobal® brand products, including the Nascobal® (Cyanocobalamin USP) nasal gel, to Questcor. The Company filed a New Drug Application ("NDA") of a nasal spray product configuration of Nascobal® in 2003 and will continue to prosecute the pending U.S. patents for the Nascobal® nasal spray product on behalf of Questcor. The Company recognized a gain of approximately \$4.2 million on the sale of the assets in 2003. The gain was calculated as \$14 million in non-contingent proceeds, less the net book value of the assets of \$8.1 million, less costs and fees. At the time of the sale, approximately \$1 million of the gain relating to the fair value of work to be completed on the filing of the NDA for the Nascobal® nasal spray product was deferred.

Under the terms of the Asset Purchase Agreement, between the Company and Questcor, Questcor paid the Company \$9 million at closing, \$3 million in September 2003 and approximately \$2.2 million in December 2003. Questcor has also agreed to make payments of: (i) \$2 million contingent upon FDA approval of a New Drug Application for the Nascobal® nasal spray product; and (ii) \$2 million contingent upon issuance of a U.S. patent for the Nascobal® nasal spray product. FDA approval for the Nascobal® nasal spray product was granted in January 2005, and the \$2 million payment was received from Questcor in February 2005.

In connection with the sale, Questcor and the Company entered into an agreement (the "Security Agreement") pursuant to which Questcor granted the Company a collateral interest in all the assets related to the Nascobal® (Cyanocobalamin USP) nasal gel acquired by Questcor.

Under the terms of a supply agreement between the parties, subject to certain limitations, the Company is obligated to manufacture and supply all of Questcor's requirements and Questcor is obligated to purchase from the Company all of its requirements, for the Nascobal® nasal gel and, upon FDA approval, the Nascobal® nasal spray. During each of the years ended December 31, 2003 and December 31, 2004, the Company recognized approximately \$300,000 of product revenue related to the supply agreement. In addition, Questcor (as successor in interest to RiboGene, Inc., Rugby Laboratories, Inc., and Darby Pharmaceuticals, Inc.) and Natestch terminated an agreement entered into in March 1990 under which Questcor, as successor in interest, purchased Natestch's Metoclopramide HCl patent and other related proprietary information (the "Metoclopramide Agreement"). The Metoclopramide Agreement provided for certain minimum royalties through October 2004, and other fees payable to Natestch if and when nasal Metoclopramide HCl is approved for marketing and commercialized. The Company received \$100,000 in 2002 as minimum royalties pursuant to this agreement.

**Pharmacia** - In January 2003, the Company entered into a divestiture agreement (the "Divestiture Agreement") with Pharmacia, under which the Company reacquired all rights to the intranasal apomorphine product that was the subject of the collaboration and license agreement that the Company and Pharmacia entered into in February 2002 (the "Pharmacia Agreement"). The Divestiture Agreement was the result of the Federal Trade Commission's ("FTC") consideration of the merger between Pfizer Inc. and Pharmacia (the "Pfizer-Pharmacia Merger"). The divestiture was intended to address concerns of the FTC's staff that the Pfizer-Pharmacia Merger could inhibit innovation and competition in the sexual dysfunction marketplace. In April 2003, the Pfizer-Pharmacia Merger closed. Effective upon the closing, the existing Pharmacia Agreement and the related Supply Agreement were terminated and the Company reacquired from Pharmacia all product and intellectual property rights granted to Pharmacia under the Pharmacia Agreement. In addition, Pharmacia granted the Company an exclusive, royalty-free license to utilize, for the treatment of human sexual dysfunction, any Pharmacia patents and know-how that relate to the intranasal apomorphine product currently under development and transferred to the Company all information relating to the development, commercialization, and marketing of this product. Also effective upon the closing of the Pfizer-Pharmacia Merger, Pharmacia and Pfizer covenanted not to sue the Company for infringement of certain patents by reason of its development or commercialization of the current product, or in certain instances, other intranasal apomorphine products, for human sexual dysfunction. Pharmacia has further covenanted that, for a period of one year following the closing of the Pfizer-Pharmacia Merger, neither it nor Pfizer will develop or commercialize an intranasal apomorphine product for the treatment of human sexual dysfunction. Pfizer agreed to

divest itself of the 250,000 shares of the Company's common stock that it purchased in connection with the Pharmacia Agreement in accordance with an agreed-upon timeframe and process.

Upon the signing of the Divestiture Agreement in January 2003, Pharmacia made a cash payment to the Company of \$13.5 million consisting of a \$6.0 million divestiture payment, \$7.0 million in research and development funds and \$500,000 for reimbursement of expenses of the divestiture transaction. During the year ended December 31, 2003, the Company recognized \$13.0 million in license and research fees and \$500,000 of legal expense reimbursement relating to the \$13.5 million payment.

Under the terms of the Pharmacia Agreement, Pharmacia had received exclusive, worldwide rights to develop and market intranasal apomorphine for the treatment of male and female sexual dysfunction and had agreed to manage and fund all future development in these indications. The Company received \$5.0 million for transfer of the apomorphine Investigational New Drug application to Pharmacia in 2002, which were deferred and amortized over the estimated development period. In 2003, the Company recognized all remaining deferred revenue from the license fees due to the termination of the Pharmacia Agreement. During the years ended December 31, 2003 and 2003, the Company recognized \$1.7 million and \$3.3 million, respectively, in license fee revenue related to these payments.

In addition to revenue recognized as license fees, the Company received \$3.0 million in 2002 for achieving certain other development milestones. Under the terms of the Pharmacia Agreement, Pharmacia also agreed to pay the Company for certain research and development costs for activities conducted by the Company since the execution of the Pharmacia Agreement. During the years ended December 31, 2002 and 2003, the Company recognized revenue of \$2.6 million and \$11,000, respectively, related to such activities, all of which is included in license and research fee revenue.

**Cytoc Corporation** - In July 2003, the Company entered into an agreement with Cytoc Corporation ("Cytoc") pursuant to which Cytoc acquired patent rights to the Company's Mammary Aspirate Specimen Cytology Test Device. Under the terms of the agreement, the Company received a license fee, and has the potential to receive milestone payments and royalties in the future.

#### **Note 14 — Related Party Transactions**

Prior to 2005, the Company paid certain monthly expenses incurred by a company that is owned and controlled primarily by its CEO in exchange for use of this company's laboratory facility for certain research and development work. Under this arrangement, during years ended December 31, 2002, 2003 and 2004, the Company paid rent of approximately \$37,000, \$32,000 and \$1,500, respectively. In January 2004, the Company entered into an agreement to sublet this facility to a third party through May 2004, the remaining term of the lease, after which there are no further obligations of the Company relating to this transaction.

Prior to 2003, a member of the Board provided legal services to the Company. Fees paid approximated \$83,000 during the year ended December 31, 2002, and zero in the years ended December 31, 2003 and December 31, 2004.

From 1999 until 2002, the Company provided split-dollar life insurance for its former Chairman of the Board of Directors (currently a director) in consideration for services provided and in lieu of cash remuneration. At the end of 15 years, the premiums the Company paid were to be repaid, with such repayment secured by the Company's collateral interest in the insurance policy. For the year ended December 31, 2002 the Company recognized \$40,000 of expense related to this policy. In January 2004, the Company and the director entered into a termination agreement whereby the Company has no future obligations with respect to the split-dollar life agreement, the Company has no right to any of the cash surrender value or proceeds of the life insurance policy and the Company will forego any existing accounts receivable it has recorded related to the Company's interest in the life insurance policy through the split-dollar life agreement. In 2003, the Company expensed approximately \$54,000 which was recorded as a receivable for the split-dollar life agreement.

In 2003, the Company entered into a consulting agreement which terminated in 2004 with a member of the Board, for strategic pharmaceutical consulting services. Under the agreement, the director was paid \$45,000 and \$60,000 in 2003 and 2004, respectively. In October 2004, the Company entered into a consulting agreement with a company associated with this director, for meeting planning services under which the company was paid \$25,000 in 2004. The services were completed in 2004 and the Company has no further obligation under the agreement.

#### **Note 15 — Capital Lease Financing**

In April 2002, the Company entered into a capital lease agreement with GE Capital Corporation (the "Lease"), which allowed it to finance certain property and equipment purchases over a three or four year term depending on the type of equipment. Under this agreement, the Company purchases assets approved by GE Capital Corporation, at which time GE Capital Corporation assumes ownership of the assets and reimburses the Company. The equipment is then leased to the Company. The original lease has been amended to allow for additional borrowings and the Company may now finance up to \$4.0 million through December 31, 2005. The Company borrowed approximately \$0.4 million, \$2.4 million and \$1.9 million in the years ended December 31, 2002, December 31, 2003 and December 31 2004, respectively. Interest rates on capital lease borrowings averaged approximately 9.8%, 8.5% and 8.9% during 2002, 2003 and 2004, respectively. Assets leased are pledged as collateral for capital lease borrowings.

#### **Note 16 — Quarterly Financial Data (Unaudited) (in thousands, except per share data)**

<b>Fiscal 2003 Quarter Ended</b>	<b>March 31, 2003</b>	<b>June 30, 2003</b>	<b>September 30, 2003</b>	<b>December 31, 2003</b>
Total revenues	\$ 2,317	\$ 15,718	\$ 494	\$ 911
Operating expenses	(5,149)	(6,918)	(6,740)	(6,844)
Gain on sale of product	—	4,236	—	—
Net income (loss)	(2,925)	12,952	(6,251)	(5,917)
Income (loss) per share – Basic	\$ (0.29)	\$ 1.26	\$ (0.58)	\$ (0.50)
Income (loss) per share – Diluted	\$ (0.29)	\$ 1.20	\$ (0.58)	\$ (0.50)

<b>Fiscal 2003 Quarter Ended</b>	<b>March 31, 2003</b>	<b>June 30, 2003</b>	<b>September 30, 2003</b>	<b>December 31, 2003</b>
Total revenues	\$ 148	\$ 45	\$ 203	\$ 1,451
Operating expenses	(7,751)	(7,485)	(7,730)	(7,372)
Net loss	(7,644)	(7,491)	(7,555)	(5,919)
Loss per share - Basic and Diluted	\$ (0.64)	\$ (0.62)	\$ (0.57)	\$ (0.41)

## ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

### ITEM 9A. CONTROLS AND PROCEDURES

(a) *Disclosure Controls and Procedures.* As of the end of the period covered by this Annual Report on Form 10-K, the Company carried out an evaluation, under the supervision and with the participation of senior management, including the Company's Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of its disclosure controls and procedures. Based upon that evaluation, the Company's Chief Executive Officer and Chief Financial Officer concluded that the Company's disclosure controls and procedures are effective for gathering, analyzing and disclosing the information that the Company is required to disclose in reports filed under the Securities Exchange Act of 1934, as amended.

(b) *Internal Control over Financial Reporting.* There have been no changes in the Company's internal controls over financial reporting or in other factors during the year ended December 31, 2004 that materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting subsequent to the date the Company carried out its most recent evaluation.

(c) *Management Report on Internal Control.* Internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, is a process designed by, or under the supervision of, the Company's chief executive officer and chief financial officer, or persons performing similar functions, and effected by the Company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's management, with the participation of the Company's chief executive officer and chief financial officer, has established and maintained policies and procedures designed to maintain the adequacy of the Company's internal control over financial reporting, and includes those policies and procedures that:

- 1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- 2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and
- 3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Management has evaluated the effectiveness of the Company's internal control over financial reporting as of December 31, 2004 based on the control criteria established in a report entitled *Internal Control—Integrated Framework*, issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). Based on our assessment and those criteria, the Company's management has concluded that the Company's internal control over financial reporting is effective as of December 31, 2004.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect all errors or misstatements and all fraud. Therefore, even those systems determined to be effective can provide only reasonable, not absolute, assurance that the objectives of the policies and procedures are met. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.



The registered independent public accounting firm of KPMG LLP has issued an attestation report on management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2004. This report appears on page 46 of this annual report on Form 10-K/A.

## **ITEM 9B. OTHER INFORMATION**

On December 14, 2004, the Company completed a public offering of 4,250,000 shares of its common stock pursuant to its \$80 million shelf registration statement, with gross proceeds of approximately \$57.4 million to the Company, prior to the deduction of fees and commissions of \$4.5 million. The underwriting agreement by and among the Company and the underwriters is being filed as exhibit 1.1 to this Annual Report on Form 10-K/A.

## **PART III**

## **ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT**

### **Directors and Executive Officers**

*Dr. Steven C. Quay.* Dr. Quay has been employed by the Company since August 2000 as Chairman of the Board, President and Chief Executive Officer. In 1999, Dr. Quay founded and was Chairman, President and Chief Executive Officer of Atossa Healthcare, Inc. ("Atossa"), which focused on the development of a proprietary platform of diagnostics and treatments related to breast cancer risk assessment and therapeutics and other healthcare products for women. We acquired Atossa in August 2000. In 1991, Dr. Quay founded Sonus Pharmaceuticals, Inc. ("Sonus"), a company engaged in the research and development of drug delivery systems and oxygen delivery products based on emulsion and surfactant technology, where he served as Chief Executive Officer, President and a director until June 1999. In 1984, Dr. Quay founded Salutar, Inc. ("Salutar") to develop contrast agents for magnetic resonance imaging. Two pharmaceuticals, OmniScan® and TeslaScan®, were invented by Dr. Quay at Salutar and are now FDA-approved for sale in the United States and other countries. Dr. Quay has authored more than 100 papers in diagnostic imaging, oncology and biochemistry and holds 48 U.S. patents. Dr. Quay graduated from the University of Michigan Medical School, where he received an M.A. and a Ph.D. in biological chemistry in 1974 and 1975, respectively, and an M.D. in 1977. Dr. Quay completed his post-graduate work in the chemistry department of Massachusetts Institute of Technology and received his residency training at Massachusetts General Hospital, Harvard Medical School in Boston. From 1980 to 1986, he was a faculty member of Stanford University School of Medicine. Dr. Quay serves as a member of the Board of Directors pursuant to an agreement with the Company set forth in his employment agreement. See "Certain Relationships and Related Transactions – Contractual Arrangements."

*J. Carter Beese, Jr.* Mr. Beese has been a director of the Company since June 2003, and currently serves as a member of the Audit, Nominating and Compensation Committees of the Board of Directors. Since July 1998, Mr. Beese has served as President of Riggs Capital Partners, a venture fund that manages in excess of \$100 million. This fund is part of Riggs National Corporation, based in Washington, D.C. He has also served as a Senior Advisor to Allied Capital Corporation since 2003. In July 2003, President George W. Bush appointed Mr. Beese to the President's Information Technology Advisory Committee. In November 2003, he was named by U.S. District Judge Rakoff and the Securities and Exchange Commission (the "SEC") as the manager of the \$250 million of MCI Inc. stock to be distributed to the victims of accounting fraud, pursuant to the Fair Fund provision of the Sarbanes-Oxley Act of 2002. Mr. Beese has also served on the board of directors of Aether Systems, Inc. since 1999, on the board of directors of Riggs National Corporation since 2001, and on the board of directors of the National Stock Exchange since 2002. Previously, Mr. Beese served on the boards of directors of Renaissance Hotel Group, a publicly traded company, from 1995 until its acquisition by Marriott International, Inc. in 1997 and of Equivest Finance, Inc., a publicly traded company, from 2001 until its acquisition by Cendant Corporation in 2002. Prior to 1999, Mr. Beese also served on numerous other public and private company boards.

*Dr. Ian R. Ferrier.* Dr. Ferrier has been a director of the Company since January 1995. Dr. Ferrier is the founder, President and Chief Executive Officer of Bogart Delafield Ferrier Inc., and has served in such capacity since its

inception in 1982. Trained in medicine and pharmacology, Dr. Ferrier has managed and directed pharmaceutical programs and guided the growth of several multinational companies. He has served on the board of directors of a number of health care and biotechnical firms, as well as serving as consultant to many of the world's major pharmaceutical companies. From 1982 to 1987, Dr. Ferrier served as President of McCann Healthcare Inc. From 1982 to 1983, Dr. Ferrier served as Chairman of The Covington Group of Companies, in 1982 as Executive Vice President of TechAmerica Group and from 1979 to 1982, as Vice President of Kalipharma Inc. From 1975 to 1979, Dr. Ferrier served as Chief Executive Officer of the Monadnock Medical Center. Dr. Ferrier received a B.Sc. in Pharmacology from the University of Edinburgh, Edinburgh, Scotland, served his residency training in nephrology/clinical pharmacology at Southmead General Hospital, University of Bristol Associated Hospitals, Bristol, England and completed a post-graduate internship at the Western General Hospital of the University of Edinburgh Associated Hospitals, Edinburgh, Scotland.

*Myron Z. Holubiak.* Mr. Holubiak has been a director of the Company since June 2004, and currently serves as a member of the Compensation Committee of the Board of Directors. Mr. Holubiak is currently a member of the board of directors of BioScrip Inc. Since 2002, Mr. Holubiak has been a partner and Group President of HealthSTAR Communications, Inc., a health care marketing communications network. From August 2001 to June 2002, Mr. Holubiak was President, Chief Operating Officer and a member of the board of directors of iPhysicianNet, Inc., a video detailing company. From December 1998 to August 2001, Mr. Holubiak served as the President of Roche Laboratories, Inc., a major research based pharmaceutical company, and was responsible for all U.S. operations including oversight of the market development and launch of the obesity product, Xenical, and the influenza product, Tamiflu. Prior to holding this position, he spent 15 years in a variety of marketing, sales and executive positions with Roche Laboratories, founded Emron, Inc., a health care consulting company, and participated in the founding of the Academy of Managed Care Pharmacy. Mr. Holubiak served on the board of directors of the Robert Wood Johnson Hospital Foundation from 1999 to 2001. He currently serves on the board of directors of the Children of Chernobyl Relief Foundation. Mr. Holubiak received a B.S. in Molecular Biology and Biophysics from the University of Pittsburgh in 1969, and did graduate work in Biophysics at the University of Pittsburgh from 1969 to 1970.

*Leslie D. Michelson.* Mr. Michelson has been a director of the Company since June 2004, and currently serves as a member of the Audit Committee of the Board of Directors. Mr. Michelson has served as Vice Chairman and Chief Executive Officer of the Prostate Cancer Foundation, the world's largest private source of prostate cancer research funding since April 2002. Mr. Michelson is currently a member of the board of directors for Catellus Development Corporation, a NYSE listed real estate investment trust. From April 2001 to April 2002, Mr. Michelson served as an investor, advisor and/or director for a portfolio of entrepreneurial health care, technology and real estate companies. From March 2000 to August 2001, Mr. Michelson served as Chief Executive Officer and as a director of Acurian, Inc., an Internet company that accelerates clinical trials for new prescription drugs. From 1999 to March 2000, Mr. Michelson served as Managing Director of Saybrook Capital, LLC, an investment bank specializing in the real estate and health care industries. From June 1998 to February 1999, Mr. Michelson served as Chairman and Co-Chief Executive Officer of Protocare, Inc., a manager of clinical trials for the pharmaceutical industry and disease management firm. From 1988 to 1998, Mr. Michelson served as Chairman and Chief Executive Officer of Value Health Sciences, Inc., an applied health services research firm. Mr. Michelson received a B.A. in Social and Behavioral Sciences from The Johns Hopkins University in 1973 and a J.D. from Yale Law School in 1976.

*John V. Pollock.* Mr. Pollock has been a director of the Company since September 1993, and currently serves as a member of the Audit, Nominating and Compensation Committees of the Board of Directors, and is Chairman of the Audit and Compensation Committees. Mr. Pollock is presently the Executive Vice President of United Bank in Vienna, Virginia. From 1975 through the present, he has been a senior banking executive and Chief Executive Officer of other banks in the Washington, D.C. area. From 1991 to 2003, Mr. Pollock served as a director of Frank E. Basil, Inc., a worldwide provider of facilities maintenance, engineering and operations maintenance services. Mr. Pollock has also served as a consultant to the partners of Basil Properties and as President of Nastech-Basil International, Inc., a joint venture between Basil Properties and the Company, which joint venture was dissolved in 1993.

*Gerald T. Stanewick.* Mr. Stanewick has been a director of the Company since June 2004. Mr. Stanewick is a private investor who spent more than 30 years on Wall Street before retiring in 2003. From 1991 through 2003, Mr. Stanewick was an institutional bond salesman with Spear Leeds & Kellogg, a subsidiary of Goldman Sachs & Co. ("Goldman Sachs"). From 1981 to 1991 he worked for Wertheim Schroder & Co. ("Wertheim") and was a partner in charge of the bond department of Wertheim's San Francisco Office from 1986 to 1991. Prior to Wertheim, Mr. Stanewick was a government bond trader with Bear Stearns. From 1976 to 1980, he was a government bond trader with Mitchell Hutchins. From 1972 to 1976, Mr. Stanewick was a securities analyst with Goldman Sachs covering Fortune 500 companies. He received a B.A. in Economics from St. Michael's College in Burlington, Vermont. Mr. Stanewick serves on the Board of Directors as the designee of Dr. Steven C. Quay, Chairman of the Board, President and Chief Executive Officer of the Company. See "Certain Relationships and Related Transactions - Contractual Arrangements."

*Bruce R. Thaw.* Mr. Thaw has been a director of the Company since June 1991. Mr. Thaw is the President and Chief Executive Officer of Bulbtronics, Inc., a national distributor of technical and specialty light sources and related products and has served in this position since 2000. Mr. Thaw is a practicing attorney and was admitted to the bar of the State of New York in 1978 and the California State Bar in 1983. From 1984 to 2001, Mr. Thaw served as general counsel to the Company. Mr. Thaw is also a director of SafeNet, Inc., a publicly traded company that designs, manufactures and markets computer network security systems and products, and Amtech Systems, Inc., a publicly traded company engaged in the semi-conductor equipment industry. Mr. Thaw holds a B.B.A. degree in Banking and Finance from Hofstra University and a J.D. degree from the Hofstra University School of Law.

*Devin N. Wenig.* Mr. Wenig served as Chairman of the Board of Directors of the Company from June 1991 to March 1999 and currently serves as a director and as a member of the Audit, Nominating and Compensation Committees of the Board of Directors, and is Chairman of the Nominating Committee. Mr. Wenig has served in various positions at Reuters Group, P.L.C. ("Reuters") since 1993. Mr. Wenig is currently an executive director on the Reuters Board of Directors and President of customer segments which are Reuters global business divisions (Sales and Trading, Research and Asset Management, Media and Enterprise). He joined Reuters in 1993 as Corporate Counsel, Reuters America. Mr. Wenig is also a director of Instinet, Inc. Before joining Reuters, Mr. Wenig was an attorney with the firm of Cravath, Swaine & Moore. Mr. Wenig received a B.A. degree from Union College and a J.D. degree from the Columbia University School of Law.

*Dr. Gordon C. Brandt.* Dr. Brandt joined the Company in November 2002. In his position of Executive Vice President Clinical Research and Medical Affairs, he oversees the drug development process from preclinical through clinical testing. From 1997 to 2002, Dr. Brandt worked at Sonus where he held the positions of Vice President, Clinical and Regulatory Affairs, and Director of Medical Affairs. At Sonus, Dr. Brandt was involved in managing all aspects of design and implementation of early and late stage clinical trial programs and submissions to regulatory authorities. Dr. Brandt graduated from Yale University with a B.S. degree in engineering science, received an M.D. from the University of California, San Francisco, and completed his residency training in internal medicine at Kaiser Hospital in San Francisco. Dr. Brandt holds one U.S. patent.

*Dr. Paul H. Johnson.* Dr. Johnson has been employed by the Company since September 2003 as Senior Vice President, Research and Development and Chief Scientific Officer. From 2001 to 2003, Dr. Johnson was Vice President, Research and Development and Chief Scientific Officer at EpiGenX Pharmaceuticals, Inc., a privately-held company focused on the development of epigenetic-based strategies to treat cancer and infectious diseases. From 1994 to 2001, Dr. Johnson served as the Head of the Cell and Molecular Biology Department and Principal Scientist in the Cancer Research Department at Berlex Biosciences ("Berlex") in Richmond, California, the U.S. research and development center for Schering AG in Germany. He also held an adjunct faculty position in the Graduate Division of Molecular Biology and Biochemistry at the University of California at Davis. From 1975 to 1994, Dr. Johnson was the Director of the Cell and Molecular Biology Laboratory at SRI International (formerly the Stanford Research Institute) and Professor of Biochemistry at Wayne State University Medical School. Dr. Johnson received a B.S. in biological sciences from the State University of New York ("SUNY"), Buffalo, a Ph.D. in biochemistry from the Roswell Park Cancer Institute (SUNY), and completed his post-doctoral training at the California Institute of Technology under an American Cancer Society fellowship.

*Gregory L. Weaver.* Mr. Weaver has been employed by the Company since May 2002 as its Chief Financial Officer. He was appointed Secretary in 2003. Prior to joining the Company, Mr. Weaver held the positions of Vice President, Strategic Development, and Vice President and Chief Financial Officer of Ilex Oncology, Inc. ("Ilex"), an oncology-focused biopharmaceutical company. During his tenure at Ilex, Mr. Weaver was involved in a series of strategic financings and acquisitions. Prior to Ilex, Mr. Weaver held several senior financial management positions, including Vice President and Chief Financial Officer of Prism Technologies, a medical device company, and Chief Financial Officer of a division of Fidelity Capital. Mr. Weaver received a B.A. in accounting from Trinity University in San Antonio, Texas, and an M.B.A. in finance from Boston College. He also served in the United States Air Force. Mr. Weaver received his Certified Public Accountant license in 1985.

*David E. Wormuth.* Mr. Wormuth has been employed by the Company since March 2001 as its Senior Vice President, Operations. From 1997 to 2001, Mr. Wormuth was President of David E. Wormuth & Associates, a consulting firm providing expert consulting services to the pharmaceutical industry related to manufacturing and quality control. From 1992 until 1997, Mr. Wormuth served as Vice President of Operations for Sonus. Prior to joining Sonus, Mr. Wormuth spent five years in various operational and manufacturing positions with Kabivitrum, Inc., a Swedish firm, specializing in emulsion technology and the development of amino acids for LVP applications. Prior to Kabivitrum, Mr. Wormuth spent 13 years with Abbott Laboratories in various manufacturing roles until 1987. Mr. Wormuth graduated from Newberry College in Newberry, South Carolina, where he received a B.A. in history and political science, and also served in the United States Marine Corps.

*Timothy M. Duffy.* Mr. Duffy has been employed by the Company since June 2004 as Vice President, Marketing and Business Development. Prior to joining the Company, Mr. Duffy held the position of Vice President, Business Development at Prometheus Laboratories Inc. ("Prometheus"), a privately held specialty pharmaceutical company. During his career at Prometheus, Mr. Duffy managed the acquisition of seven pharmaceutical products, the licensing of nine diagnostic technologies, and the negotiation of other transactions. Prior to Prometheus, Mr. Duffy served for 13 years in functional and management positions in the pharmaceutical division at The Procter & Gamble Company. Mr. Duffy received a B.A. in biology from Loras College in Dubuque, Iowa.

#### **Identification of the Audit Committee**

The Audit Committee, which currently consists of directors John V. Pollock, Chairman, J. Carter Beese, Jr., Leslie D. Michelson and Devin N. Wenig, held nine meetings during 2004. Among other functions, the Audit Committee authorizes and approves the engagement of the independent registered public accountants, reviews the results and scope of the audit and other services provided by the independent registered public accountants, reviews the Company's financial statements, reviews and evaluates the Company's internal control functions, approves or establishes pre-approval policies and procedures for all professional audit and permissible non-audit services provided by the independent registered public accountants and reviews and approves any proposed related party transactions.

The Board of Directors has determined that each of John V. Pollock, J. Carter Beese, Jr., Leslie D. Michelson and Devin N. Wenig is an independent director within the meaning of the Nasdaq independence standards and Rule 10A-3 promulgated by the SEC under the Exchange Act. In addition, the Board of Directors has determined that each member of the Audit Committee qualifies as an Audit Committee Financial Expert under applicable SEC Rules and satisfies the Nasdaq standards of financial literacy and financial or accounting expertise or experience.

#### **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), requires the Company's executive officers, directors and persons who beneficially own more than 10% of the Company's Common Stock to file initial reports of ownership and reports of changes in beneficial ownership with the SEC. Such persons are required by SEC regulations to furnish the Company with copies of all Section 16(a) forms filed by such persons. Based solely on its review of copies of such forms received by it, or written representations from

certain reporting persons, the Company believes that, with respect to 2004, all the Company's executive officers and directors, and all persons known to the Company to beneficially own more than 10% of the Company's Common Stock, complied with all such reporting requirements.

### **Code of Business Conduct and Ethics**

The Board of Directors has three standing committees: the Audit Committee, the Compensation Committee and the Nominating Committee. The Board of Directors has adopted a Code of Business Conduct and Ethics applicable to all employees, officers and directors, which the Company makes available free of charge on or through its internet website. The Company's internet website is [www.nastech.com](http://www.nastech.com). The Company intends to disclose on its internet website any amendments to or waivers from its Code of Business Conduct and Ethics. Any stockholder also may obtain a copy of the Company's Code of Business Conduct and Ethics, free of charge, by sending a request in writing to: Nastech Pharmaceutical Company Inc., Investor Relations Department, 3450 Monte Villa Parkway, Bothell, Washington 98021.

## **ITEM 11. EXECUTIVE COMPENSATION**

### **Compensation of Directors**

In 2004, each non-employee director was paid an annual fee of \$3,000, plus \$1,500 for each Board of Directors' meeting attended and \$750 for each committee meeting attended, and was reimbursed for travel expenses incurred to attend such meetings.

*Directors' Stock Option Plans.* The Company maintains three compensation plans under which equity compensation awards may be made to directors: the Amended and Restated Nastech Pharmaceutical Company Inc. 2000 Nonqualified Stock Option Plan (the "2000 Plan"), the Nastech Pharmaceutical Company Inc. 2002 Stock Option Plan (the "2002 Plan") and the Nastech Pharmaceutical Company Inc. 2004 Stock Incentive Plan (the "2004 Plan"). References to the "Director Option Plans" herein refer to the 2000 Plan, the 2002 Plan and the 2004 Plan, collectively. It is the Company's current practice that, upon becoming a member of the Board of Directors, each non-employee director may receive a discretionary award of options to purchase Common Stock and/or restricted shares of Common Stock as is determined at such time by the Compensation Committee of the Board of Directors. The discretionary stock option grants under the Director Option Plans are made at an exercise price per share of no less than the "fair market value" (as defined under the Director Option Plans) of a share of Common Stock on the date the option is granted, and both discretionary stock option and restricted stock grants are generally subject to a vesting period determined by the Compensation Committee in accordance with the applicable Director Option Plan (under most circumstances, a one-year vesting period, or, for certain stock option grants under the 2004 Plan, the earlier of the first anniversary of the date of grant or the date of the next annual meeting of the Company's stockholders). The Compensation Committee may make additional discretionary grants to eligible directors, consistent with the terms of the Director Option Plans. The Board of Directors may amend, suspend or terminate the Director Option Plans at any time, except that prior approval of the Company's stockholders must be obtained pursuant to applicable Nasdaq rules for any amendments that would constitute a material revision to any of the Director Option Plans, and certain changes require the consent of the affected grantees. In 2004, 75,000 options and 61,500 shares of restricted Common Stock were granted to the non-employee members of the Board of Directors pursuant to the Director Option Plans.

## 2004 Director's Compensation

Director	Cash Fees
J. Carter Beese, Jr. ....	\$ 22,500
Dr. Ian R. Ferrier .....	\$ 12,000
Myron Z. Holubiak .....	\$ 10,500
Leslie D. Michelson .....	\$ 10,875
John V. Pollock .....	\$ 22,875
Gerald T. Stanewick .....	\$ 10,875
Bruce R. Thaw .....	\$ 16,125
Devin N. Wenig(1) .....	\$ 19,125
Total .....	<u>\$ 124,875</u>

(1) From 1999 until 2002, the Company provided split-dollar life insurance for Devin Wenig, its former Chairman of the Board of Directors (and current director) in consideration for services rendered as Chairman of the Board of Directors and in lieu of cash remuneration. When the insurance policy was purchased, the Company agreed to pay the premiums on the split-dollar life insurance policy and at the end of 15 years, the premiums the Company paid were to be repaid to it, with such repayment secured by the Company's collateral interest in the insurance policy. In January 2004, the Company and Mr. Wenig agreed to terminate the arrangement. As a result, the Company has no future obligations with respect to the payment of a premium in the amount of \$39,659 per year under the split-dollar life insurance policy and it has no right to any of the cash surrender value or proceeds of the split-dollar life insurance policy. The Company's receivable that was forfeited upon termination of the arrangement with Mr. Wenig was \$158,638.

## Executive Compensation

The following table sets forth certain information regarding compensation paid by the Company during each of the Company's last three years to (i) the person who served as the Company's Chief Executive Officer during 2004 and (ii) the four most highly compensated executive officers of the Company other than the Chief Executive Officer who were serving as executive officers as of December 31, 2004 and whose total salary and bonus exceeded \$100,000 in 2004.

## Summary Compensation Table

Name and Principal Position	Year	Annual Compensation			Long-Term Compensation			
		Salary (\$)	Bonus(\$)	Other Annual Compensation	Awards		Payouts	
					Restricted Stock Awards(\$)	Securities Underlying Options/Warrants(#)	LTIP Payouts	All Other Compensation(\$)
Dr. Steven C. Quay .....	2004	393,250	200,000	-	-	-	-	-
Chairman, President and	2003	357,500	50,000	-	-	-	-	-
Chief Executive Officer	2002	316,927	25,000	-	-	900,000(6)	-	-
Dr. Gordon C. Brandt .....	2004	224,750	73,800	-	-	-	-	-
Executive Vice President Clinical	2003	200,000	80,250	-	-	25,000(7)	-	-
Research and Medical Affairs (1)	2002	20,498	56,667	-	-	90,000(8)	-	-
Dr. Paul H. Johnson .....	2004	249,832	56,280	-	-	-	-	-
Senior Vice President, Research	2003	51,539	22,000	-	-	90,000(9)	-	-
and Development and Chief							-	-
Scientific Officer (2)								
Gregory L. Weaver .....	2004	250,000	100,000	-	84,300(5)	7,500(10)	-	-
Chief Financial Officer (3)	2003	242,796	97,149	-	-	25,000(11)	-	-
	2002	146,087	47,846	100,000(4)	-	125,000(12)	-	-
David E. Wormuth .....	2004	228,275	74,874	-	-	25,000(13)	-	-
Senior Vice President,	2003	207,428	83,008	-	-	25,000(14)	-	-
Operations	2002	192,476	79,056	-	-	10,000(15)	-	-

- (1) Dr. Brandt commenced employment with the Company in November 2002.
- (2) Dr. Johnson commenced employment with the Company in September 2003.
- (3) Mr. Weaver commenced employment with the Company in May 2002.
- (4) Represents relocation expenses paid to Mr. Weaver in connection with the commencement of his employment in 2002 and his relocation to the Company's offices in Bothell, Washington.
- (5) One June 9, 2004, Mr. Weaver was awarded 7,500 shares of restricted Common Stock pursuant to the Company's 2004 Incentive Stock Plan. The value of such restricted stock is based upon a \$11.24 stock price, which was the closing price of the Common Stock on the date of grant. One-third of the shares vest on each of the first three anniversary dates of the grant. These shares of restricted Common Stock are eligible to receive dividends, however, the Company has no current plans to pay any dividends.
- (6) Includes options to purchase 800,000 shares of the Common Stock at an exercise price of \$12.94 per share, and options to purchase 100,000 shares of Common Stock at an exercise price of \$25.00 per share. See "Executive Compensation – Employment Contracts, Termination of Employment and Change in Control Arrangements."
- (7) Represents options to purchase 25,000 shares of Common Stock at an exercise price of \$8.89 per share.
- (8) Represents options to purchase 90,000 shares of Common Stock at an exercise price of \$10.99 per share.
- (9) Represents options to purchase 90,000 shares of Common Stock at an exercise price of \$9.36 per share.
- (10) Represents options to purchase 7,500 shares of Common Stock at an exercise price of \$11.24 per share. See "Executive Compensation – Option Grants in 2004."
- (11) Represents options to purchase 25,000 shares of Common Stock at an exercise price of \$8.21 per share.
- (12) Represents options to purchase 125,000 shares of Common Stock at an exercise price of \$15.30 per share. See "Executive Compensation – Employment Contracts, Termination of Employment and Change in Control Arrangements."
- (13) Represents options to purchase 25,000 shares of Common Stock at an exercise price of \$13.90 per share. See "Executive Compensation – Option Grants in 2004."
- (14) Represents options to purchase 25,000 shares of Common Stock at an exercise price of \$8.21 per share.
- (15) Represents options to purchase 10,000 shares of Common Stock at an exercise price of \$13.63 per share.

## Option Grants in 2004

The following table provides the specified information concerning grants of options to purchase Common Stock during 2004 to the executive officers named in the Summary Compensation Table. The Company did not issue stock appreciation rights in 2004.

Name	Individual Grants in 2004			Expiration Date	Potential Realizable Value at Assumed Annual Rates of Appreciation for Option Term (3)	
	Number of Securities Underlying Options Granted (#)(1)	% of Total Options Granted to Employees in 2004	Exercise or Base Price (\$/Share) (2)		5%(\$)	10%(\$)
Dr. Steven C. Quay .....	—	—	—	—	—	—
Dr. Gordon C. Brandt.....	—	—	—	—	—	—
Dr. Paul H. Johnson .....	—	—	—	—	—	—
Gregory L. Weaver.....	7,500	5.3%	11.24	06/09/14	53,016	134,352
David E. Wormuth .....	25,000	17.8%	13.90	04/14/14	218,540	553,826

- (1) One-third of the shares subject to the options granted to Mr. Weaver and Mr. Wormuth vest on each of the first three anniversaries of the date of grant.
- (2) Options granted at market value on the date of grant.
- (3) Potential realizable value represents hypothetical gains that could be achieved for the options if exercised at the end of the option terms assuming that the Common Stock appreciates at the annual rate shown, compounded annually, from the date of grant until the expiration of the option term. The assumed 5% and 10% rates of stock price appreciation are provided in accordance with rules of the SEC and do not represent an estimate or projection of the future price of the Common Stock. Actual gains, if any, on stock option exercises will depend on the future performance of the Common Stock.

## Aggregated Option Exercises in 2004 and Year-End Option Values

The following table provides information regarding the number and value of stock options exercised during 2004 by the executive officers named in the Summary Compensation Table. The table also provides information regarding the number and value of unexercised in-the-money options held at the end of 2004.

	Shares Acquired on Exercise	Value Realized (\$)	Number of Securities Underlying Unexercised Options at December 31, 2004		Value of Unexercised In-the-Money Options at December 31, 2004 (a)	
			Exercisable	Unexercisable	Exercisable (\$)	Unexercisable (\$)
Dr. Steven C. Quay .....	90,000	861,900	1,006,719	300,000	874,819	0
Dr. Gordon C. Brandt.....	—	—	68,334	46,666	93,352	86,798
Dr. Paul H. Johnson .....	—	—	30,000	60,000	82,200	164,400
Gregory L. Weaver .....	—	—	91,668	65,832	32,419	71,281
David E. Wormuth .....	7,500	64,395	82,501	44,999	536,982	64,831

- (a) Market value of shares subject to in-the-money options on December 31, 2004, less option exercise price. Options are in-the-money if the market value of the shares subject to the options is greater than the option exercise price.



## Employment Contracts, Termination of Employment and Change in Control Arrangements

*Dr. Steven C. Quay.* The employment agreement of the Company's President, Chief Executive Officer and Chairman, Dr. Steven C. Quay, originally due to expire on August 8, 2003, was amended and restated effective May 2, 2002. Pursuant to the amended agreement, Dr. Quay will receive base compensation of \$325,000 per year, with increases of 10% per year beginning on January 1, 2003. Dr. Quay's base compensation was increased to \$357,500 effective January 1, 2003, was increased to \$393,250 effective January 1, 2004 and was increased to \$432,575 effective January 1, 2005. Dr. Quay is also entitled to annual incentive cash compensation to be paid based on the achievement of certain performance levels in each of several performance areas agreed upon by the Company and Dr. Quay prior to the commencement of each year. The incentive cash compensation is targeted for \$100,000 per year and limited to \$200,000 per year, with the actual amount determined by the Board of Directors or the Compensation Committee. The amended and restated agreement expires on December 31, 2005 unless it is extended by written agreement between the parties. The Company, through the Compensation Committee of the Board of Directors, is currently negotiating a new employment agreement with Dr. Quay. If Dr. Quay remains in substantially full-time employment by the Company beyond December 31, 2005 without such a written extension, his employment (and his employment agreement) shall be deemed to continue on a month-to-month basis, with either party having the right to terminate his employment at the end of any calendar month upon 30 days written notice.

In connection with the original employment agreement, Dr. Quay received options to purchase 600,000 shares of Common Stock at four different exercise prices which equaled or exceeded \$4.09, the market price of the Common Stock on the date of grant, as summarized in the following table:

<u>Exercise price</u>	<u>Number of shares</u>
\$ 4.09 .....	226,719
\$ 4.50 .....	73,281
\$12.00 .....	200,000
\$15.00 .....	100,000

Pursuant to the May 2002 amendment to Dr. Quay's employment agreement, Dr. Quay was granted additional options to purchase 800,000 shares of Common Stock at an exercise price of \$12.94 per share, which equaled the market price of the Common Stock on the date of grant. The grant was approved by stockholders on June 6, 2002. The option vests as follows: (i) 200,000 options vested on execution of the amended employment agreement, (ii) 200,000 options vested on August 8, 2003, (iii) 200,000 options vested on August 8, 2004 and (iv) 200,000 options vest on August 8, 2005. In addition, Dr. Quay was granted an option to purchase an additional 100,000 shares of Common Stock at an exercise price of \$25.00 per share which will vest on January 1, 2006, if and only if, on or before December 31, 2005, the Company and Dr. Quay agree in writing upon terms for Dr. Quay's continued service as President and Chief Executive Officer of the Company until at least December 31, 2007.

The amended and restated employment agreement also provides that the Company will, in connection with each election of directors of the Company during the term of the agreement, nominate, recommend and use its best efforts to cause the election to the Board of Directors of Dr. Quay and a person designated by Dr. Quay who is reasonably acceptable to the Company. The Company is also obligated to use all best efforts to cause the election of Dr. Quay as Chairman of the Board of Directors.

In the event that, prior to December 31, 2005, the Company terminates Dr. Quay's employment without cause or Dr. Quay is constructively terminated by the Company, Dr. Quay will be entitled to receive as severance the amount of base compensation that would have been payable to Dr. Quay through December 31, 2005, computed using the base salary rate in effect on the date of termination. Upon such event, the vesting and exercisability of the options to purchase 900,000 shares of Common Stock granted pursuant to the amended agreement and the option to purchase 600,000 shares of Common Stock granted pursuant to Dr. Quay's original employment agreement dated August 8, 2000, will be immediately and fully accelerated. For these purposes, a constructive termination means (i) a demotion or substantial diminution of responsibilities, (ii) a failure by the Company to honor its obligations under the agreement or (iii) prior to August 8, 2005, either Dr. Quay or Dr. Quay's designee (if any) is not elected to the

Board of Directors, or Dr. Quay is not elected as Chairman of the Board, unless, in the case of Dr. Quay's designee only, the lost election was the result of votes against the designee by non-affiliate stockholders of the Company representing the majority of the votes cast.

In the event that, prior to December 31, 2005, Dr. Quay's employment is terminated due to disability or death, Dr. Quay or his estate, as applicable, is entitled to receive as severance the lesser of twelve months base compensation or the compensation that would have been payable to Dr. Quay through December 31, 2005, computed using the base salary rate in effect on the date of termination.

In the event that, during the one-year period following a change in control of the Company and prior to December 31, 2005, Dr. Quay's employment is terminated by the Company or by Dr. Quay for any reason, Dr. Quay will be entitled to receive as severance an amount equal to the greater of twelve months base compensation at the rate in effect on the date of termination or the base compensation payable during the remainder of the term of the agreement, and an additional payment equal to the sum of the pro-rated incentive cash compensation for the year in which he is terminated plus the full amount of targeted incentive cash compensation for the following year. Dr. Quay is also entitled to an additional gross-up payment to cover any "golden parachute" excise taxes that may be payable by Dr. Quay upon receipt of these severance payments. In addition, the vesting and exercisability of the options granted to Dr. Quay under the amended agreement and the original agreement will be immediately and fully accelerated. Pursuant to the agreement, a change in control generally means (i) the acquisition by any person or group of 40% or more of the Company's voting securities, (ii) the Company's reorganization or merger or sale of all or substantially of the Company's assets, following which the Company's stockholders prior to the consummation of such reorganization, merger or sale hold 60% or less of the voting securities of the surviving or acquiring entity, as applicable, (iii) a turnover of the majority of the Board of Directors as currently constituted, provided that under most circumstances any individual elected by a majority of the incumbent Board of Directors shall be considered as a member of the incumbent Board of Directors for this purpose, or (iv) a complete liquidation or dissolution of the Company.

*Gregory L. Weaver.* The Company and Gregory L. Weaver, the Company's Chief Financial Officer, are parties to an employment agreement dated April 30, 2002. The agreement provides that Mr. Weaver shall receive an annual base salary of \$235,000 commencing May 20, 2002, which was increased to \$250,000 for 2004 and to \$280,000 effective as of January 1, 2005, and provided for a grant of 125,000 stock options which shall vest over a 3 year period. These stock options were granted with an exercise price of \$15.30 per share, which was the closing price of the Common Stock on the date of grant. Under the agreement, Mr. Weaver is entitled to receive annual incentive compensation of up to 40% of the applicable base salary if certain performance objectives are met (the "Executive Bonus Plan"). The Company and Mr. Weaver are also parties to a Change-In-Control Severance Agreement, dated July 31, 2002, which provides for certain benefits in the event that Mr. Weaver's employment is terminated without cause, or his employment is constructively terminated, within one year following a change in control of the Company. In such event, the Company is obligated to pay severance in an amount equal to the sum of Mr. Weaver's annual base salary on the date of termination plus his target incentive compensation for that year under the Executive Bonus Plan. In addition, the vesting and exercisability of all stock options then held by Mr. Weaver will be fully accelerated. For purposes of this agreement, a change in control generally means (i) the acquisition by any person or group of 50% or more of the Company's voting securities, (ii) the Company's reorganization or merger, or sale of all or substantially of the Company's assets, following which the Company's stockholders prior to the consummation of such reorganization, merger or sale hold 60% or less of the voting securities of the surviving or acquiring entity, as applicable, (iii) a turnover of the majority of the Board of Directors as currently constituted, provided that under most circumstances any individual elected by a majority of the incumbent Board of Directors shall be considered as a member of the incumbent Board of Directors for this purpose, or (iv) a complete liquidation or dissolution of the Company. A constructive termination means (i) a demotion or substantial diminution of responsibilities, or (ii) a decrease in annual base salary below \$235,000.

## **Report of Compensation Committee on Executive Compensation**

Notwithstanding anything to the contrary set forth in any of the Company's previous filings under the Securities Act or the Exchange Act that might incorporate future filings, including this Proxy Statement, in whole or in part, the following report and the Performance Graph which follows shall not be deemed to be incorporated by reference into any such filings.

### *Executive Compensation Philosophy*

The Company's Compensation Committee is composed entirely of independent, outside directors. Its functions include establishing the general compensation policies of the Company, reviewing and approving compensation for the executive officers, and administering the Company's stock option plans. One important goal that the Company has for the Compensation Committee is to have the members of the committee design compensation packages for executive officers of the Company sufficient to attract and retain persons of exceptional quality, and to provide effective incentives to motivate and reward such executives for achieving the scientific, financial and strategic goals of the Company essential to the Company's long-term success and growth in stockholder value. The Company's typical executive compensation package has historically consisted of three main components: (1) base salary; (2) incentive cash bonuses; and (3) stock options and restricted stock grants. From time to time, the Compensation Committee may retain compensation and other management consultants to assist with, among other things, structuring the Company's various compensation programs and determining appropriate levels of salary, bonus and other compensatory awards payable to the Company's executive officers and other employees, as well as to guide the Company in the development of near-term and long-term individual performance objectives established by the Compensation Committee.

### *Base Compensation*

The Compensation Committee's approach is to offer executive salaries competitive with those of other executives in the industry in which the Company operates. To that end, the Compensation Committee evaluates the competitiveness of its base salaries based upon information drawn from various sources, including published and proprietary survey data, consultants' reports and the Company's own experience recruiting and training executives and professionals. The Company's base salary levels are intended to be consistent with competitive practice and such executive's level of responsibility. Base salaries will be reviewed annually and may be increased by the Compensation Committee in accordance with certain performance criteria including, without limitation, (i) individual performance, (ii) Company performance, (iii) the functions performed by the executive officer and (iv) changes in the compensation peer group in which the Company competes for executive talent. The weight given such factors by the Compensation Committee may vary from individual to individual.

### *Bonuses*

In addition to base salary, executives and managers are eligible to receive discretionary bonuses, from time to time, upon the achievement of certain scientific, financial and other business milestones related to Company and individual performance. At the beginning of each year, the Compensation Committee and the Company's chief executive officer review each individual's job responsibilities and goals for the upcoming year. The amount of the bonus and any performance criteria vary with the position and role of the individual within the Company. For the year ended December 31, 2004, discretionary incentive and merit cash bonuses in recognition of services performed were awarded to executive officers as follows: \$200,000 to Dr. Steven C. Quay, \$73,800 to Dr. Gordon C. Brandt, \$56,280 to Dr. Paul H. Johnson, \$100,000 to Gregory L. Weaver and \$74,874 to David E. Wormuth.

### *Employee Stock Option Plans*

The Company maintains three compensation plans under which equity compensation awards may be made to employees: the 2000 Plan, the 2002 Plan and the 2004 Plan (collectively herein, the "Employee Option Plans"). Awards are granted under the Employee Option Plans based on a number of factors, including (i) the executive

officer's or key employee's position in the Company, (ii) his or her performance and responsibilities, (iii) the extent to which he or she already holds an equity stake in the Company, (iv) equity participation levels of comparable executives and key employees at other companies in the compensation peer group and (v) individual contribution to the success of the Company's financial performance. However, the Employee Option Plans do not provide any formulated method for weighing these factors, and a decision to grant an award is based primarily upon the evaluation by the Compensation Committee, in consultation with the Company's chief executive officer, of the past as well as the future anticipated performance and responsibilities of the individual in question.

Historically, the Company, from time to time, has granted stock options and other stock awards in order to provide certain executives with a competitive total compensation package and to reward them for their contribution to the long-term price performance of the Company's Common Stock. Grants of stock options and other stock awards are designed to align the executive's interest with that of the stockholders of the Company. In addition, to assist the Company in retaining employees and encouraging them to seek long-term appreciation in the value of the Company's stock, awards generally are not exercisable immediately upon grant, but instead vest over a specified period. Accordingly, an employee must remain with the Company for a specified period to enjoy the full economic benefit of an award.

In 2004, the Compensation Committee approved equity compensation awards under the Company's Employee Option Plans to executive officers of the Company as follows: (i) on April 14, 2004, David E. Wormuth was granted options to purchase 25,000 shares of Common Stock at an exercise price of \$13.90 per share, which shall vest in three equal annual installments on each of the first three anniversary dates of the grant, (ii) on June 9, 2004, Gregory L. Weaver was awarded 7,500 shares of restricted Common Stock and granted options to purchase 7,500 shares of Common Stock at an exercise price of \$11.24 per share, which options and restricted shares shall vest in three equal annual installments on each of the first three anniversary dates of the grant, and (iii) on June 9, 2004, Timothy M. Duffy was awarded 15,000 shares of restricted Common Stock and granted options to purchase 15,000 shares of Common Stock at an exercise price of \$11.24 per share, which options and restricted shares shall vest in three equal annual installments on each of the first three anniversary dates of the grant.

#### *401(k) Savings Plan*

The Company maintains a tax-qualified 401(k) savings and profit sharing plan for its eligible employees (the "401(k) Plan"). Employees who have attained the age of 21 and completed at least three months and at least 250 hours of service with the Company are eligible to elect to defer up to the lesser of \$13,000 during calendar year 2004 (\$14,000 during calendar year 2005) or 100% of their base pay on a pre-tax basis. Participants age 50 and older may make additional pre-tax contributions to the 401(k) Plan of up to \$3,000 during calendar year 2004 (\$4,000 during calendar year 2005). The Company may make discretionary matching or profit sharing contributions to the 401(k) Plan on behalf of eligible participants in any plan year, as may be determined by the Board of Directors. For calendar year 2004, the Board of Directors decided to match employee pre-tax contributions of up to 6% of compensation at 25 cents for each dollar contributed by the employee. Accordingly, the Company made discretionary matching contributions of \$79,000 to the 401(k) Plan for calendar year 2004, including matching contributions for executive officers as follows: \$3,344 for Dr. Gordon C. Brandt, \$500 for Dr. Paul H. Johnson, \$2,909 for Gregory L. Weaver and \$1,846 for David E. Wormuth.

#### *Chief Executive Officer Compensation*

Dr. Steven C. Quay, the Chairman of the Board, President and Chief Executive Officer of the Company, received a base salary during 2004 of \$393,250 pursuant to terms and conditions of his employment agreement entered into in August 2000, as amended and restated in May 2002. Dr. Quay also was paid a cash bonus of \$200,000 in recognition of services performed during fiscal 2004. Dr. Quay received no fees for his service as a director of the Company during fiscal 2004. The Compensation Committee recognizes Dr. Quay's contributions to the Company's operations and attempts to ensure that the President and Chief Executive Officer's compensation is commensurate with the compensation of chief executive officers of comparable corporations. The Board of Directors deemed such bonus and Dr. Quay's total compensation appropriate in light of his substantial contribution

to the Company's growth and success in 2004. Dr. Quay's base compensation was increased to \$432,575 effective January 1, 2005. In addition, the Company, through the Compensation Committee of the Board of Directors, is currently negotiating a new employment agreement with Dr. Quay.

#### COMPENSATION COMMITTEE

John V. Pollock, Chairman

J. Carter Beese, Jr.

Myron Z. Holubiak

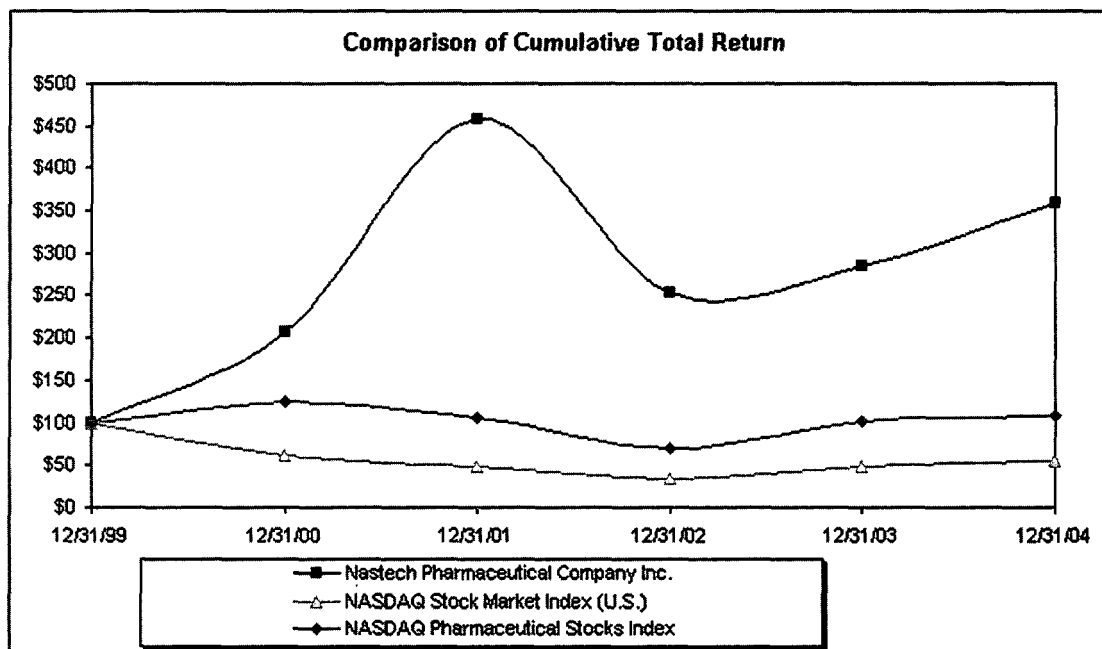
Devin N. Wenig

#### Compensation Committee Interlocks and Insider Participation

The Company's Compensation Committee is currently composed of Directors Pollock, Beese, Holubiak and Wenig. No executive officer of the Company serves as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of the Company's Board of Directors or Compensation Committee.

#### Comparison of Stock Performance

The following graph compares the cumulative total return on the Company's Common Stock with the cumulative total return of the Nasdaq Composite Index and the Nasdaq Pharmaceutical Index for the period beginning on January 1, 2000 and ending on December 31, 2004. The graph assumes an investment of \$100 on December 31, 1999 in the Company's Common Stock and in each of the indices, and the reinvestment of all dividends, if any. The stockholder return shown on the graph below is not necessarily indicative of future performance, and the Company will not make or endorse any predictions as to future stockholder returns.



	12/31/99	12/31/00	12/31/01	12/31/02	12/31/03	12/31/04
Nastech Pharmaceutical Company Inc.	100.0	207.1	458.6	253.0	284.3	358.0
NASDAQ Stock Market Index (U.S.) NASDAQ	100.0	60.3	47.8	33.1	49.4	53.8
Pharmaceutical Stocks Index	100.0	124.7	106.3	68.7	100.7	107.2

## ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

### Security Ownership of Certain Beneficial Owners and Management

Set forth below is certain information as of March 31, 2005 for (i) the members of the Board of Directors, (ii) the executive officers of the Company and (iii) the directors and executive officers of the Company as a group. Except as otherwise set forth below, there are no persons or groups that are known by the Company to beneficially own more than 5% of the Company's outstanding shares of Common Stock. Unless otherwise indicated, the business address of each person in the table below is c/o Nastech Pharmaceutical Company Inc., 3450 Monte Villa Parkway, Bothell, Washington 98021.

<u>Name and Position</u>	<u>Age</u>	<u>First Elected</u>	<u>Current Term Expires</u>	<u>Number of Shares(1)</u>	<u>Percent of Shares Outstanding %(1)</u>
Dr. Steven C. Quay, Chairman of the Board, President and Chief Executive Officer (2).....	54	2000	2005	1,793,940 (7)	9.5%
Dr. Gordon C. Brandt, Executive Vice President Clinical Research and Medical Affairs.....	45	—	—	75,834 (8)	*
Dr. Paul H. Johnson, Senior Vice President, Research and Development and Chief Scientific Officer .....	62	—	—	34,000 (9)	*
Gregory L. Weaver, Chief Financial Officer and Secretary.....	49	—	—	141,834 (10)	*
David E. Wormuth, Senior Vice President, Operations.....	59	—	—	94,168 (11)	*
Timothy M. Duffy, Vice President, Marketing and Business Development .....	44	—	—	15,000 (12)	*
J. Carter Beese, Jr., Director (3)(4)(5).....	48	2003	2005	61,000 (13)	*
Dr. Ian R. Ferrier, Director .....	62	1995	2005	16,000 (14)	*
Myron Z. Holubiak, Director (5) .....	58	2004	2005	30,000 (15)	*
Leslie D. Michelson, Director (3).....	54	2004	2005	36,500 (16)	*
John V. Pollock, Director (3)(4)(5) .....	66	1993	2005	104,333 (17)	*
Gerald T. Stanewick, Director (6) .....	58	2004	2005	178,668 (18)	*
Bruce R. Thaw, Director.....	52	1991	2005	229,541 (19)	1.3%
Devin N. Wenig, Director (3)(4)(5).....	38	1991	2005	416,987 (20)	2.3%
All directors and executive officers as a group.....	—	—	—	3,227,805 (21)	16.4%

\* Beneficial Ownership of less than 1.0% is omitted.

- (1) Except as otherwise noted below, includes all outstanding shares of Common Stock, shares of Common Stock underlying vested options or vested warrants, and all outstanding restricted shares of Common Stock (both vested and unvested), that are owned beneficially by the individual listed with sole voting and/or investment power. All references to "vested" options or "vested warrants" shall include all such options or warrants that are exercisable as of March 31, 2005, as well as those options or warrants that will become exercisable within 60 days of March 31, 2005.
- (2) Pursuant to the terms and conditions of Dr. Quay's amended and restated employment agreement with the Company, the Company has agreed, for the term of Dr. Quay's employment with the Company, that the Company will nominate Dr. Quay and a designee of his choice, each for successive terms as a member of the Board of Directors. The Company has nominated Gerald T. Stanewick as Dr. Quay's designee for election to the Board of Directors. See "Certain Relationships and Related Transactions – Contractual Arrangements."
- (3) Member of the Audit Committee of the Board of Directors.
- (4) Member of the Nominating Committee of the Board of Directors.

- (5) Member of the Compensation Committee of the Board of Directors.
- (6) The Company has nominated Gerald T. Stanewick as Dr. Quay's designee for election to the Board of Directors. See "Certain Relationships and Related Transactions – Contractual Arrangements."
- (7) Includes vested options to purchase 1,006,719 shares of Common Stock and 193,281 shares of Common Stock directly beneficially owned by Dr. Quay. Also includes 593,940 shares held by K-Quay Enterprises LLC, of which Dr. Quay is a beneficial owner. Does not include unvested options to purchase 200,000 shares of Common Stock that will vest on August 8, 2005 and options to purchase 100,000 shares of Common Stock which will vest on January 1, 2006, if and only if, on or before December 31, 2005, the Company and Dr. Quay agree in writing upon terms for Dr. Quay's continued service as President and Chief Executive Officer of the Company until at least December 31, 2007.
- (8) Includes vested options to purchase 68,334 shares of Common Stock and 7,500 unvested restricted shares of Common Stock.
- (9) Includes vested options to purchase 30,000 shares of Common Stock and 4,000 unvested restricted shares of Common Stock.
- (10) Includes vested options to purchase 133,334 shares of Common Stock and 7,500 unvested restricted shares of Common Stock.
- (11) Includes vested options to purchase 94,168 shares of Common Stock.
- (12) Includes 15,000 unvested restricted shares of Common Stock.
- (13) Includes vested options to purchase 58,000 shares of Common Stock and 3,000 unvested restricted shares of Common Stock.
- (14) Includes vested options to purchase 13,000 shares of Common Stock and 3,000 unvested restricted shares of Common Stock.
- (15) Includes vested options to purchase 15,000 shares of Common Stock and 15,000 unvested restricted shares of Common Stock.
- (16) Includes vested options to purchase 15,000 shares of Common Stock and 16,500 unvested restricted shares of Common Stock.
- (17) Includes vested options to purchase 88,000 shares of Common Stock and 3,000 unvested restricted shares of Common Stock.
- (18) Includes vested options to purchase 15,000 shares of Common Stock, vested warrants to purchase 10,256 shares of Common Stock and 15,000 unvested restricted shares of Common Stock. Also includes 57,500 shares of Common Stock held by Mr. Stanewick's spouse.
- (19) Includes vested options to purchase 128,500 shares of Common Stock and 3,000 unvested restricted shares of Common Stock.
- (20) Includes vested options to purchase 48,000 shares of Common Stock and 3,000 unvested restricted shares of Common Stock.

- (21) Includes vested options to purchase 1,713,055 shares of Common Stock, vested warrants to purchase 10,256 shares of Common Stock, and 95,500 unvested restricted shares of Common Stock.

### Equity Compensation Plan Information

The following chart provides aggregate information as of December 31, 2004 about Common Stock that may be issued (i) upon the exercise of options under all of the Company's equity compensation plans, including the Nastech Pharmaceutical Company Inc. 1990 Stock Option Plan (the "1990 Plan"), the 2000 Plan, the 2002 Plan and the 2004 Plan, and (ii) upon the exercise of options granted to certain executive officers as inducement awards made pursuant to such officers' employment agreements, which shares are covered by a Registration Statement on Form S-8.

	(a)	(b)	(c)
	Number of securities to be issued upon exercise of outstanding options	Weighted-average exercise price of outstanding options	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders	1,623,000(1)	\$ 11.82	491,880
Equity compensation plans not approved by security holders	1,136,252(2)	\$ 10.71	126,990
Total	2,759,252	\$ 11.36	618,870

- (1) Consists of 260,500 shares of Common Stock underlying awards made pursuant to the 1990 Plan and 1,362,500 shares of Common Stock underlying awards made pursuant to the 2002 Plan. The Board of Directors has delegated authority to the Compensation Committee to serve as administrator of the 1990 Plan, the 2002 Plan and the 2004 Plan.
- (2) Consists of 664,533 shares of Common Stock underlying awards made pursuant to the 2000 Plan, and 471,719 shares of Common Stock underlying options awarded to Dr. Steven C. Quay and Gregory L. Weaver as an inducement to enter into their respective employment agreements with the Company in August 2000 and May 2002, respectively. Under the 2000 Plan, the Company is authorized to grant non-qualified stock options to purchase a maximum of 1,000,000 shares of Common Stock (subject to adjustment in the event of stock splits, stock dividends, recapitalization and other capital adjustments) to the Company's employees, officers, directors and consultants. The Board of Directors has delegated authority to the Compensation Committee to serve as administrator of the 2000 Plan. The Compensation Committee has discretion as to the persons to be granted options, the number of shares subject to the options and the vesting schedules of the options. The 2000 Plan also provides that options shall be exercisable during a period of no more than ten years from the date of grant, and that the option exercise price shall be at least equal to 100% of the fair market value of the Common Stock on the date of grant.

### ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Certain directors and executive officers of the Company (or members of their immediate families or related trusts) had direct or indirect interests in certain transactions involving the Company in the last fiscal year as set forth below. In accordance with applicable Nasdaq rules and the Company's Code of Business Conduct and Ethics applicable to all directors, officers and employees of the Company, all related party transactions were reviewed and approved by the Audit Committee of the Board of Directors.

In October 2003, the Company entered into a consulting agreement with Dr. Ian Ferrier, a member of the Board of Directors, for the purpose of advising the company on its strategic planning. Under the agreement, Dr. Ferrier was paid \$60,000 in 2004. The agreement terminated on April 30, 2004. In October 2004, the Company entered into a consulting agreement with an entity associated with Dr. Ferrier, for meeting planning services under which the



entity was paid \$25,000 in 2004. The services were completed in 2004 and the Company has no further obligations under the agreement.

## **ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

### **Independent Registered Public Accountant Services and Fees**

KPMG LLP served as the Company's independent registered public accountants for the year ended December 31, 2004 and has been the Company's independent registered public accountants for each completed fiscal year beginning with the year ended December 31, 1996. Total fees billed to the Company by KPMG LLP for the years ended December 31, 2004 and 2003 were \$264,000 and \$159,296, respectively, and were comprised of the following:

*Audit Fees.* The aggregate fees billed for professional services rendered in connection with (i) the audit of the Company's annual financial statements, (ii) the review of the financial statements included in the Company's Quarterly Reports on Form 10-Q for the quarters ended March 31, June 30 and September 30, (iii) consents and comfort letters issued in connection with equity offerings and (iv) services provided in connection with statutory and regulatory filings or engagements were \$245,000 for the year ended December 31, 2004 and \$139,296 for the year ended December 31, 2003.

*Audit-Related Fees.* The Company did not incur any audit-related fees for the years ended December 31, 2004 and December 31, 2003.

*Tax Fees.* The aggregate fees billed for professional services rendered in connection with tax compliance, tax planning and federal and state tax advice were \$19,000 for the year ended December 31, 2004 and \$20,000 for the year ended December 31, 2003.

*All Other Fees.* The Company did not incur any other fees for the years ended December 31, 2004 and December 31, 2003.

### **Pre-Approval Policies and Procedures**

Pursuant to its charter, the Audit Committee has the sole authority to appoint or replace the Company's independent registered public accountants (subject, if applicable, to stockholder ratification). The Audit Committee is directly responsible for the compensation and oversight of the work of the independent registered public accountants (including resolution of disagreements between management and the independent registered public accountants regarding financial reporting) for the purpose of preparing or issuing an audit report or related work. The independent registered public accountants are engaged by, and report directly to, the Audit Committee.

The Audit Committee pre-approves all auditing services and permitted non-audit services (including the fees and terms thereof) to be performed for the Company by its independent registered public accountants, subject to the *de minimis* exceptions for non-audit services described in Section 10A(i)(1)(B) of the Exchange Act and SEC Rule 2-01(c)(7)(i)(C) of Regulation S-X, provided that all such excepted services are subsequently approved by the Audit Committee prior to the completion of the audit. In the event pre-approval for such auditing services and permitted non-audit services cannot be obtained as a result of inherent time constraints in the matter for which such services are required, the Chairman of the Audit Committee has been granted the authority to pre-approve such services, provided that the estimated cost of such services on each such occasion does not exceed \$15,000, and the Chairman of the Audit Committee reports for ratification such pre-approval to the Audit Committee at its next scheduled meeting. The Audit Committee has complied with the procedures set forth above, and has otherwise complied with the provisions of its charter.

**PART IV**

**ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

*(a)(1) Financial Statements and Financial Statement Schedule*

The financial statements and schedule listed in the Index to Financial Statements are filed as part of this Form 10-K/A.

*(a)(3) Exhibits*

The exhibits required by this item are set forth on the Exhibit Index attached hereto.

## **SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Bothell, State of Washington, on April 29, 2005.

### **NASTECH PHARMACEUTICAL COMPANY INC.**

By: /s/ Steven C. Quay

Steven C. Quay, M.D., Ph.D.

Chairman of the Board, President and Chief Executive Officer

## EXHIBIT INDEX

Exhibit No.	Description
1.1	Underwriting Agreement dated December 8, 2004, by and among Natestch Pharmaceutical Company Inc. and Citigroup Global Markets Inc., Needham & Company, Inc., WR Hambrecht + Co., LLC and Delafield Hambrecht, Inc. for themselves and as representatives of the underwriters (filed as Exhibit 1.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 filed with the Securities and Exchange Commission on March 8, 2005, and incorporated herein by reference).
2.1	Agreement and Plan of Reorganization, dated August 8, 2000, among the Company, Atossa Acquisition Corporation, a Delaware corporation and wholly-owned subsidiary of the Company, and Atossa HealthCare, Inc. (filed as Exhibit 2.1 to the Company's Current Report on Form 8-K dated August 8, 2000, and incorporated herein by reference).
2.2	Asset Purchase Agreement, dated September 30, 2002, with Schwarz Pharma, Inc. (filed as Exhibit 2.1 to the Company's Current Report on Form 8-K dated September 30, 2002 and incorporated herein by reference).
3.1	Certificate of Incorporation of the Company dated September 20, 1983 (filed as Exhibit 3.1 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.2	Certificate of Amendment to the Certificate of Incorporation of the Company dated November 30, 1989 (filed as Exhibit 3.2 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.3	Certificate of Amendment to the Certificate of Incorporation of the Company dated November 8, 1993 (filed as Exhibit 3.3 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.4	Certificate of Amendment to the Certificate of Incorporation of the Company dated December 30, 1996 (filed as Exhibit 3.4 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.5	Certificate of Amendment to the Certificate of Incorporation of the Company dated August 15, 1999 (filed as Exhibit 3.5 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.6	Certificate of Designation of Rights, Terms and Preferences of Series A Junior Participating Preferred Stock of the Company dated March 2, 2000 (filed as Exhibit A to our Current Report on Form 8-K dated February 22, 2000 and incorporated herein by reference).
3.7	Certificate of Correction to a Certificate of Amendment to the Certificate of Incorporation of the Company dated July 28, 2004 (filed as Exhibit 3.7 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.8	Certificate of Correction to a Certificate of Amendment to the Certificate of Incorporation of the Company dated July 28, 2004 (filed as Exhibit 3.8 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.9	Certificate of Correction to a Certificate of Amendment to the Certificate of Incorporation of the Company dated July 28, 2004 (filed as Exhibit 3.9 to our Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
3.10	Amended and Restated Bylaws of the Company dated August 11, 2004 (filed as Exhibit 3.10 to our

<u>Exhibit No.</u>	<u>Description</u>
	Registration Statement on Form S-3, File No. 333-119429, and incorporated herein by reference).
4.1	Investment Agreement, dated as of February 1, 2002, by and between the Company and Pharmacia & Upjohn Company (filed as Exhibit 4.1 to the Company Current Report on Form 8-K dated February 1, 2002 and incorporated herein by reference).
4.2	Rights Agreement, dated February 22, 2000, between the Company and American Stock Transfer & Trust Company as Rights Agent (filed as Exhibit 1 to our Current Report on Form 8-K dated February 22, 2000 and incorporated herein by reference).
4.3	Securities Purchase Agreement dated as of June 25, 2004 (filed as Exhibit 99.2 to our Current Report on Form 8-K dated June 25, 2004 and incorporated herein by reference).
4.4	Form of Warrant (filed as Exhibit 99.3 to the Company's Current Report on Form 8-K dated June 25, 2004 and incorporated herein by reference).
10.1	Lease for facilities at 45 Davids Drive, Hauppauge, NY (filed as Exhibit 10B to the Company's Annual Report on Form 10-KSB for the year ended June 30, 1995 and incorporated herein by reference).
10.2	Lease Agreement, dated April 23, 2002, with Phase 3 Science Center LLC, Ahwatukee Hills Investors LLC and J. Alexander's LLC (filed as Exhibit 10.26 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2002 and incorporated herein by reference).
10.3	Amended and Restated Employment Agreement, dated May 2, 2002, with Steve C. Quay, M.D., Ph.D. (filed as Exhibit 10.27 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2002 and incorporated herein by reference).
10.4	Employment Agreement with Gregory L. Weaver, dated April 30, 2002 (filed as Exhibit 10.29 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended June 30, 2002 and incorporated herein by reference).
10.5	Change-in-Control Severance Agreement with Gregory L. Weaver, dated July 31, 2002 (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2002 and incorporated herein by reference).
10.6	Nastech Pharmaceutical Company Inc. 1990 Stock Option Plan (filed as Exhibit 4.2 to the Company's Registration Statement on Form S-8, File No. 333-28785, and incorporated herein by reference).
10.7	Amended and Restated Nastech Pharmaceutical Company Inc. 2000 Nonqualified Stock Option Plan (filed as Exhibit 4.4 to the Company's Registration Statement on Form S-8, File No. 333-49514, and incorporated herein by reference).
10.8	Nastech Pharmaceutical Company Inc. 2002 Stock Option Plan (filed as Exhibit 10.28 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended June 30, 2002 and incorporated herein by reference).
10.9	Nastech Pharmaceutical Company Inc. 2004 Incentive Stock Plan (filed as Exhibit 99 to the Company's Registration Statement on Form S-8, File No. 333-118206, and incorporated herein by reference).
10.10	Termination and Mutual Release Agreement, dated September 30, 2002, with Schwarz Pharma, Inc. (Filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated September 30, 2002 and incorporated herein by reference).
10.11	Divestiture Agreement, dated January 24, 2003, with Pharmacia & Upjohn Company (filed as Exhibit 10.1

Exhibit No.	Description
	to the Company's Current Report on Form 8-K dated January 24, 2003 and incorporated herein by reference).
10.12	Stock option agreement with Gregory L. Weaver (filed as Exhibit 10.25 to the Company's Annual Report on Form 10-K for the year ended December 31, 2002 and incorporated herein by reference).
10.13	Asset Purchase Agreement, dated June 16, 2003, by and between the Company and Questcor Pharmaceuticals, Inc. (filed as Exhibit 2.1 to the Company's Current Report on Form 8-K dated June 17, 2003 and incorporated herein by reference).
10.14	First Amendment dated June 17, 2003, to Lease Agreement dated April 23, 2002, with Phase 3 Science Center LLC, Ahwatukee Hills Investors LLC and J. Alexander's LLC (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter ended June 30, 2003 and incorporated herein by reference).
10.15	Form of Purchase Agreement (filed as Exhibit 99.2 to the Company's Current Report on Form 8-K dated September 4, 2003 and incorporated herein by reference).
10.16	Form of Warrant (filed as Exhibit 99.3 to the Company's Current Report on Form 8-K dated September 4, 2003, and incorporated herein by reference).
10.17	Revolving Line of Credit Agreement with Wells Fargo Bank, dated December 19, 2003 (filed as Exhibit 10.20 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 and incorporated herein by reference).
10.18	Addendum to Promissory Note with Wells Fargo Bank, dated January 20, 2004 (filed as Exhibit 10.21 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 and incorporated herein by reference).
10.19	Security Agreement Securities Account with Wells Fargo Bank, dated December 19, 2003 (filed as Exhibit 10.22 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 and incorporated herein by reference).
10.20	Addendum to Security Agreement: Securities Account with Wells Fargo Bank, dated December 19, 2003 (filed as Exhibit 10.23 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 and incorporated herein by reference).
10.21	Second Amendment, dated February 4, 2004, to Lease Agreement dated April 23, 2002, with Phase 3 Science Center LLC, Ahwatukee Hills Investors LLC and J. Alexander's LLC (filed as Exhibit 10.24 to the Company's Annual Report on Form 10-K for the year ended December 31, 2003 and incorporated herein by reference).
10.22	Exclusive Development, Commercialization and License Agreement by and between Merck & Co., Inc. and the Company effective as of September 24, 2004 (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated September 24, 2004 and incorporated herein by reference). (1)
10.23	Supply Agreement by and between the Company and Merck & Co., Inc. effective as of September 24, 2004 (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated September 24, 2004 and incorporated herein by reference). (1)
10.24	Revolving Line of Credit Agreement with Wells Fargo Bank, dated October 20, 2004 (filed as Exhibit 10.29 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 and incorporated herein by reference).

<u>Exhibit No.</u>	<u>Description</u>
10.25	License and Supply Agreement by and between Par Pharmaceutical, Inc. and Natestch Pharmaceutical Company Inc. effective as of October 22, 2004 (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 22, 2004 and incorporated herein by reference). (1)
10.26	Restricted Stock Grant Agreement effective January 21, 2005 by and between Natestch Pharmaceutical Company Inc. and Mr. Gordon Brandt, M.D. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated January 21, 2005 and incorporated herein by reference).
10.27	Stock Option Agreement dated as of January 21, 2005 between Natestch Pharmaceutical Company Inc. and Mr. Gordon Brandt, M.D. (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated January 21, 2005 and incorporated herein by reference).
10.28	Restricted Stock Grant Agreement effective January 21, 2005 by and between Natestch Pharmaceutical Company Inc. and Mr. Paul H. Johnson, Ph.D. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated January 21, 2005 and incorporated herein by reference).
10.29	Stock Option Agreement dated as of January 21, 2005 between Natestch Pharmaceutical Company Inc. and Mr. Paul H. Johnson, Ph.D. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated January 21, 2005 and incorporated herein by reference).
23.1	Consent of KPMG LLP, independent registered public accounting firm. (2)
31.1	Certification of the Company's Chairman of the Board, President and Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 under the Securities Exchange Act of 1934, as amended. (2)
31.2	Certification of the Company's Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 under the Securities Exchange Act of 1934, as amended. (2)
32.1	Certification of the Company's Chairman of the Board, President and Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. (2)
32.2	Certification of the Company's Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. (2)

(1) Portions of this exhibit have been omitted pursuant to a request for confidential treatment under Rule 24b-2 of the Securities Exchange Act of 1934, amended, and the omitted material has been separately filed with the Securities and Exchange Commission.

(2) Filed Herewith.

CHIEF EXECUTIVE OFFICER CERTIFICATION

REQUIRED BY RULES 13A-14 AND 15D-14 UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS AMENDED

I, Steven C. Quay, M.D., Ph.D., Chairman of the Board, President and Chief Executive Officer of Nastech Pharmaceutical Company Inc., certify that:

1. I have reviewed this annual report on Form 10-K/A of Nastech Pharmaceutical Company Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:
  - a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation;
  - d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):
  - a) all significant deficiencies in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: April 29, 2005

By: /s/ Steven C. Quay

-----  
Name: Steven C. Quay, M.D., Ph.D.  
Title: Chairman of the Board, President  
and Chief Executive Officer



CHIEF FINANCIAL OFFICER CERTIFICATION

REQUIRED BY RULES 13A-14 AND 15D-14 UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS AMENDED

I, Gregory L. Weaver, Chief Financial Officer of Nastech Pharmaceutical Company Inc., certify that:

1. I have reviewed this annual report on Form 10-K/A of Nastech Pharmaceutical Company Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:
  - a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures as of the end of the period covered by this report based on such evaluation;
  - d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):
  - a) all significant deficiencies in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: April 29, 2005

By: /s/ Gregory L. Weaver

-----  
Name: Gregory L. Weaver  
Title: Chief Financial Officer

CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Steven C. Quay, M.D., Ph.D., Chairman of the Board, President and Chief Executive Officer of Nastech Pharmaceutical Company Inc. ("Nastech"), certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Nastech on Form 10-K for the year ended December 31, 2004 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and that information contained in the Annual Report on Form 10-K/A fairly presents in all material respects the financial condition and results of operations of Nastech.

Date: April 29, 2005

By: /s/ Steven C. Quay

-----  
Name: Steven C. Quay, M.D., Ph.D.  
Title: Chairman of the Board, President  
and Chief Executive Officer

A signed original of this written statement required by Section 906 has been provided to Nastech and will be retained by Nastech and furnished to the Securities Exchange Commission or its staff upon request.

This certification accompanies each periodic report pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and shall not, except to the extent required by the Sarbanes-Oxley Act of 2002, be deemed filed by Nastech for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Gregory L. Weaver, Chief Financial Officer of Natestch Pharmaceutical Company Inc. ("Natestch"), certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Natestch Pharmaceutical Company Inc. on Form 10-K for the year ended December 31, 2004 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and that information contained in the Annual Report on Form 10-K/A fairly presents in all material respects the financial condition and results of operations of Natestch.

Date: April 29, 2005

By: /s/ Gregory L. Weaver

-----  
Name: Gregory L. Weaver

Title: Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to Natestch and will be retained by Natestch and furnished to the Securities Exchange Commission or its staff upon request.

This certification accompanies each periodic report pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and shall not, except to the extent required by the Sarbanes-Oxley Act of 2002, be deemed filed by Natestch for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

**This Page Intentionally Left Blank**

**This Page Intentionally Left Blank**

---

## **BOARD OF DIRECTORS**

**Steven C. Quay, M.D., Ph.D.**  
Chairman of the Board, President &  
Chief Executive Officer

**Susan B. Bayh, Esq. (nominee)**  
**J. Carter Beese, Jr.**  
**Alexander D. Cross, Ph.D. (nominee)**  
**Dr. Ian R. Ferrier**  
**Myron Z. Holubiak**  
**Leslie D. Michelson**  
**John V. Pollock**  
**Gerald T. Stanewick**  
**Bruce R. Thaw, Esq.**  
**Devin N. Wenig, Esq.**

## **EXECUTIVE MANAGEMENT**

**Steven C. Quay, M.D., Ph.D.**  
Chairman of the Board, President &  
Chief Executive Officer

**Gordon C. Brandt, M.D.**  
Executive Vice President, Clinical  
Research & Medical Affairs

**Timothy M. Duffy**  
Vice President, Marketing  
and Business Development

**Paul H. Johnson, Ph.D.**  
Senior Vice President, Research &  
Development and Chief Scientific Officer

**Gregory L. Weaver**  
Chief Financial Officer & Secretary

**David E. Wormuth**  
Senior Vice President, Operations

## **FORWARD-LOOKING STATEMENT**

This Annual Report contains  
forward-looking statements and  
readers should carefully review the  
risk factors in Form 10-K  
included herein.

## **REGISTRAR AND TRANSFER AGENT**

American Stock Transfer & Trust Co.  
59 Maiden Lane  
New York, N.Y. 10038  
Toll-free: 1-877-777-0800

## **LEGAL COUNSEL**

Pryor Cashman Sherman & Flynn LLP  
410 Park Avenue  
New York, N.Y. 10022

## **INDEPENDENT AUDITORS**

KPMG LLP  
801 Second Avenue  
Seattle, WA 98104

## **PUBLIC RELATIONS**

## **INVESTOR RELATIONS**

Noonan Russo  
200 Madison Avenue, 7th Fl.  
New York, N.Y. 10016  
212-845-4235

## **MEDIA RELATIONS**

Burns McClellan, Inc.  
470 Park Avenue South, 9th Fl.  
New York, N.Y. 10016  
212-213-0006

## **STOCK LISTING**

The Company's Common Stock is traded  
on the Nasdaq National Market System  
under the symbol NSTK.

## **ANNUAL MEETING**

July 20, 2005  
9:00 a.m.  
The University Club  
1 West 54th Street  
New York City

## **ANNUAL REPORT ON FORM 10-K**

The Company's Annual Report on Form  
10-K, filed with the Securities and Exchange  
Commission, is available without charge by  
writing, phoning, or visiting our website at  
[www.nastech.com](http://www.nastech.com).



**N A S T E C H**

**PHARMACEUTICAL COMPANY INC.**

Company Headquarters:  
3450 Monte Villa Parkway  
Bothell, Washington 98021  
Phone: 425-908-3600  
Fax: 425-908-3650  
[www.nastech.com](http://www.nastech.com)